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THE FORMATION, REGRESSION, AND DIFFERENTIAL DIAGNOSIS OF TRUE INFARCTS OF THE PLACENTA

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THE incentive for the study of placentas, fetal membranes, and gravid uteri by a general pathologist was initiated, about four years ago, by certain problems connected with an interdepartmental study of hypertension at the Cincinnati General Hospital. The immediate interest pertained to the vascular changes in cases of eclamptogenic toxemia. In order to evaluate properly the lesions in such cases, comparable tissues were obtained from patients with normal pregnancy and also from those in whom gestation or delivery was complicated by one or more of a wide variety of abnormal conditions. A report on this study by Zeek and Assali was published in 1950.[1]

While this material was being studied, it became evident that the nodular lesions commonly found in placentas and termed "placental infarcts" in medical literature often appeared to be of diverse nature microscopically. Among them was one type of lesion which presented all of the diagnostic features of true infarcts, as defined in general pathology. In the series of observed cases this lesion occurred with far greater frequency in those of eclamptogenic toxemia than in the nontoxemic ones.[1]

The present report gives a comparison of this lesion, in its various stages of formation and regression, with infarcts elsewhere in the body, and criteria for the differential diagnosis between this lesion and other nodules in the placenta which have commonly been called "infarcts" erroneously. It is deemed unnecessary to include a review of the voluminous literature on the subject, since

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reports and textbooks by Williams,[2] Eastman,[3] Dieckmann,[4] Montgomery,[5] Hellman,[6] Bartholomew,[7] Clements,[8] and many others provide comprehensive discussions of the various concepts expressed in this analysis.

Material and Methods

Through the cooperation of the Department of Obstetrics and the House Staff of the Cincinnati General Hospital, and the pathologists in other hospitals of the Greater Cincinnati area, specimens were obtained from over 600 cases of pregnancy. Among these were 562 entire placentas with fetal membranes and umbilical cords. Also included were specimens of uterus with the placenta and fetus in situ, other uteri removed soon after delivery, and autopsy reports, together with microscopic sections and occasionally gross specimens of viscera, from cases of maternal and fetal deaths. The present report is concerned mainly with placentas, but certain placental lesions can be understood more readily when considered in relation to pathological changes e'sewhere in the body.

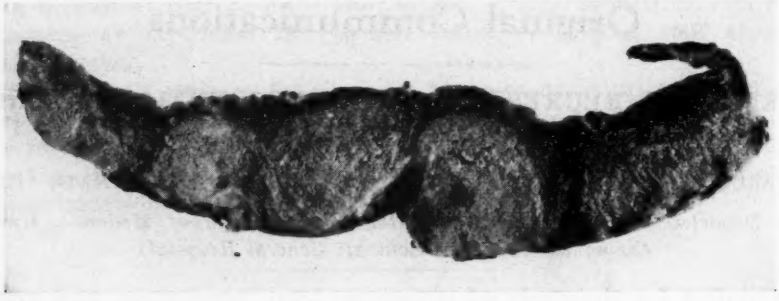


Fig. 1.—Nodular ischemia of the placenta in a case of premature separation at 32 weeks' gestation. Fetus died at birth.

The specimens were usually placed in 10 per cent formalin promptly after delivery. Following fixation they were cross-sectioned at about 1 cm. intervals, descriptions of lesions were recorded, and sections were taken for microscopic study. The paraffin-hematoxylin-eosin method was used routinely but was supplemented frequently by fat stains on frozen sections, and occasionally by other special stains on paraffin sections, particularly those used to demonstrate collagen and reticulum.

Criteria

In general pathology the term "infarct" is used to designate a localized area of necrosis caused by obstruction of its nutritional blood supply. The obstruction usually occurs rapidly, otherwise collateral circulation, fibrous replacement, and other factors produce a lesion which is not characterized by necrosis and therefore is not called an infarct. The most reliable morphological criteria of necrosis are nuclear changes which are designated karyorrhexis, karyolysis, and pyknosis. Unless one or more of these changes are visible microscopically in most of the parenchymal cells of a given area, the lesion is not an acute infarct. The inflammatory reaction which follows the onset of necrosis is always limited to the junction zone between the dead and the living tissues, since neutrophils do not invade deeply into tissues deprived of oxygen. All necrotizing inflammatory lesions are not infarcts because in some of them there is no vascular obstruction.

In most viscera the sequence of morphological changes in the formation of an infarct may be divided into the following overlapping stages:

Stage I. Prenecrotic Stage.—Immediately following sudden interference with the nutritional blood supply to an area, the part becomes pale and of increased density because of the collapse of many small vessels.

Fig. 2.—Nodular ischemia of the placenta in a case of maternal death from subarachnoid hemorrhage, with a live fetus in utero, 7 months' gestation. (×12.)

Stage II. Acute (Red) Infarct.—Promptly there ensue a dilatation and filling of the unobstructed vessels of any collateral or dual circulations in the part, thus producing the so-called red infarct. When such vessels are thin walled and poorly supported they frequently rupture, permitting infiltration of the tissues with many red blood cells, for example, in hemorrhagic infarcts of the lungs. This process of "stuffing with red cells" explains the coining of the term "infarctions" (infarcire, to stuff).[9] In tissues which have no dual or collateral circulation infarcts do not become red but remain ischemic until organized.

Stage III. Subacute Infarct.—The tissues in the ischemic area rapidly undergo necrosis, nuclear changes appearing first in the more highly differ-

entiated parenchymal cells and last in stromal cells which seem to be less sensitive to anoxia. Following the onset of necrosis neutrophilic reaction and often hyperemia occur at the margins of the dying tissue, producing a grayish-yellow ring or a double yellow and red ring around the lesion, which by this time is fading (first appearing pink, then yellow and finally gray) as the erythrocytes become hemolyzed. Their pigment is released and finally absorbed. The necrosis is usually coagulative in type and faint outlines of the original structures may remain visible for several days.

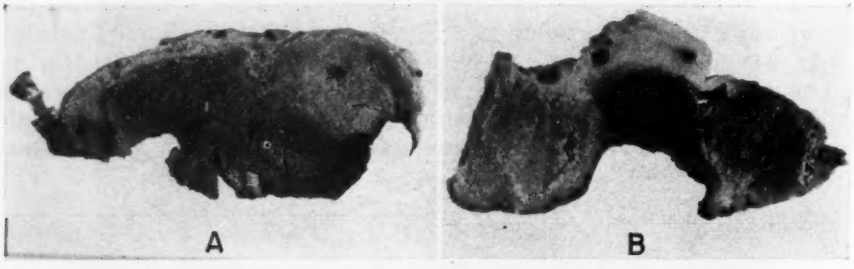


Fig. 3.—Acute (red) infarcts in a case of abruptio placentae.

A, Red infarct (on left) and nodular ischemia (on right) becoming a red infarct at the margins.

B, Nodular ischemia and two red infarcts in different stages. The concavity contained a retroplacental blood clot.

Stage IV. Old Infarct.—Healing usually occurs by the ingrowth of new capillaries and fibrocytes from the surounding living tissues. Scar formation follows collagenization of the fibrous tissue which finally replaces the original parenchyma in the involved area. Occasionally, according to the location in the body, the scar may become calcified, as in the lung, or cystic liquefaction of the dead area may occur without much proliferation of granulation tissue, as in the brain. Also, in the brain, poorly supported contiguous vessels may rupture into the dead tissue, producing massive hemorrhage.

Since it takes time for an infarct to form, a given specimen may present vascular occlusion without infarction. Pulmonary infarction is often absent in cases of terminal pulmonary embolism. In the kidney it takes about 48 hours for complete necrosis to occur. Moreover, in regions where there is a well-developed collateral or dual circulation, infarction may be prevented or arrested before complete necrosis has occurred. For this reason infarcts of the liver are rare. In some viscera, for example, in the kidney, obstruction of large veins is also effective in producing infarction by causing inadequate oxygenation of the tissues.

Observations

In a previous report[1] data were presented in support of the concept that the placenta is nourished directly from the maternal circulation and not by way of the fetal blood supply. In the present study of over 600 pregnancies there were 11 cases in which sudden cessation of the maternal blood supply to the placenta occurred while the fetus was alive in utero. Three of these were cases of sudden maternal death from extrauterine causes, the one illustrated (Fig. 2)* being a case of massive subarachnoid hemorrhage caused by rupture

*In each of the illustrations of this report the top of the section is toward the chorionic plate. All of the microscopic sections were paraffin-hematoxylin-eosin preparations.

of a congenital aneurysm of the circle of Willis. In the other eight cases there was massive retroplacental hemorrhage shortly before delivery (Fig. 1). The gross and microscopic changes in the placentas were similar in the 11 cases except that in those of maternal death all of the cotyledons were involved, while in the other eight the lesions were limited to those portions of the placenta which were separated from the uterine wall by fresh blood clot. It seems reasonable to consider the placental lesions to be described as representing the prenecrotic stage of infarction in these cases. The process did not develop further because of the death of both mother and fetus in 3 cases and prompt delivery in the other 8 cases.

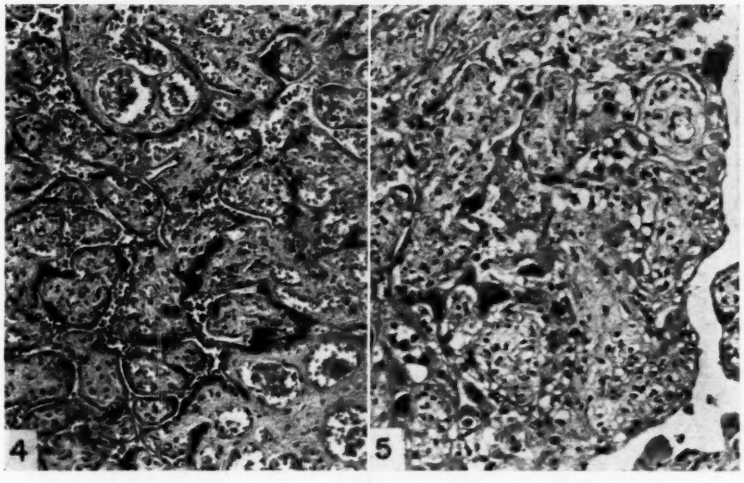


Fig. 4.—Acute (red) infarct. Dilated villous capillaries. (×160.)
Fig. 5.—Margin of subacute infarct with neutrophilic reaction. (×160.)

Infarction of the Placenta.—

Stage I: Grossly, the placentas in these 11 cases presented varying numbers of pale nodules of slightly increased density, each of which was in contact with the maternal surface of the placenta (Fig. 1). In general, the nodules corresponded in size and configuration to the normal cotyledon architecture except that they did not usually extend to the chorionic plate but terminated abruptly in the subchorionic region. The uninvolved subchorionic blood space and its extensions to the maternal surface between the cotyledons were filled with dark red venous blood. Microscopically (Fig. 2), the ischemic nodules consisted of normal-appearing chorionic villi which lay very close together because the intervillous spaces were empty and collapsed. There was no necrosis, therefore these lesions were not frank infarcts. They probably represented the prenecrotic stage of the process as outlined above. Very frequently one or more similar ischemic but nonnecrotic nodules were observed in other placentas which presented multiple true infarcts in various stages of formation and regression. The fact that the nodules were quite spongy and of only slightly increased density differentiated them grossly from other pale nodules encountered in the present study. They were often difficult to recognize microscopically until observed under very low power, when the regular, selective distribution of the collapsed intervillous spaces appeared characteristic and nonartifactual.

The other stages of placental infarction were more readily recognizable and have been described by other observers. All true infarcts observed in the

present study were found to be in contact with the maternal surface when serial sections were made. Therefore placental nodules in any other position would not be called infarcts, by the present authors, without microscopic confirmation.

Stage II: Acute placental infarcts appeared grossly as dark red, round or oval nodules of increased density, extending partially or entirely through the thickness of the placenta to the chorionic plate (Fig. 3). They varied also in width but usually did not extend beyond the cotyledon in which they took origin.

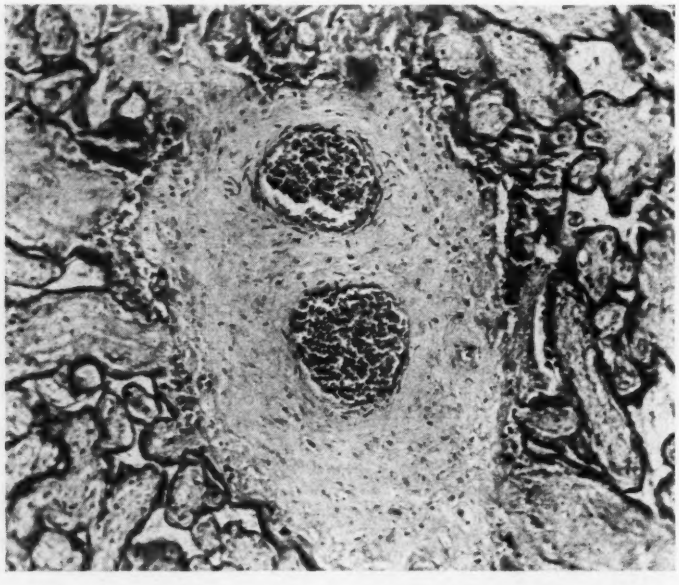


Fig. 6.—Well-preserved fetal blood in cotyledon vessels near center of a subacute infarct. (×160.)

Microscopically, the trophoblastic cells presented the early nuclear changes of necrosis. The intervillous spaces were collapsed or filled with clotted blood and the compact chorionic villi often appeared to be glued together (Fig. 4). Villous capillaries were widely dilated and filled with well-preserved fetal blood which gave the characteristic red color to the lesion. In the present series acute red infarcts were much less common than subacute yellowish ones, probably because the red stage is a transient phase of short duration and occurs only while the fetus is alive in utero. Red infarcts were usually associated with fresh retroplacental hemorrhages which had separated the placenta from its maternal blood supply, or were found together with infarcts of other ages in cases of eclamptogenic toxemia.

Stage III: Subacute infarcts were firm, pinkish or yellowish-gray nodules and were often surrounded by a yellowish reaction zone. Microscopically there was marked necrosis of villi, hemolysis of villous blood, and a zone of neutrophils at the margin of the lesion (Fig. 5). Interesting to note was the frequent presence of a few neutrophils in the stroma of the heavier cotyledon stalks deep in the areas of necrosis, the latter having not yet extended through the more resistant collagen tissue to the larger fetal blood vessels in which were well-preserved red cells and from which the neutrophils had migrated to the necrotic margins (Fig. 6).

Hemorrhages were comon in subacute infarcts. When small they were situated deeply in the lesions at considerable distances from the maternal circulation and in proximity to larger cotyledon stalks. Occasionally nucleated red

cells were present in the fresh clot. Serial sections of lesions of this nature revealed rupture of fetal vessels and spilling of well-preserved blood cells (Fig. 7), showing that the fetal circulation in the heavier cotyledon stalks may be maintained for a time after all contiguous villi, at a given level, have become necrotic. Moreover, these observations indicate that at least some of the hemorrhages into infarcts are fetal in origin. In cases of toxemia not infrequently there were massive hemorrhages in direct continuity with retroplacental hematomas, thus suggesting that fetal hemorrhage into softened necrotic infarcts may initiate retroplacental hemorrhage which, if massive, may be an important factor in the causation of fetal death in utero, and of severe anemia in the newborn.

Stage IV: The process of placental infarction prior to this stage was very similar to that of infarctions elsewhere in the body, but the healing process was

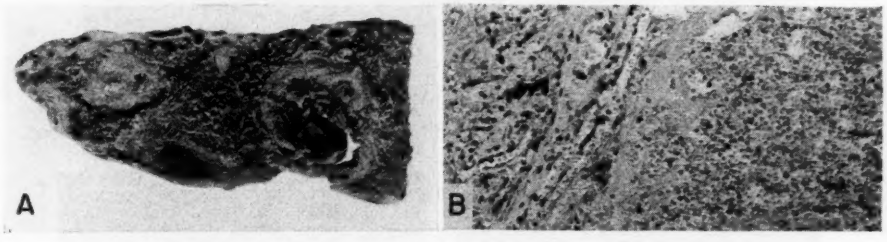
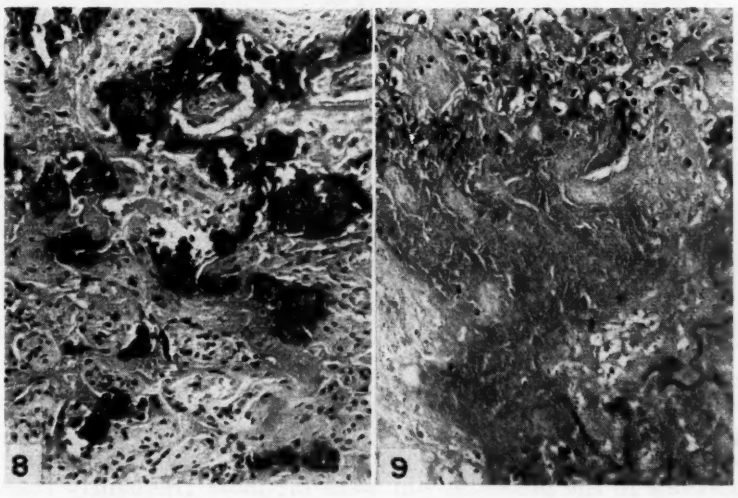


Fig. 7.—Fetal hemorrhage into a subacute infarct of the placenta.

A, Subacute infarcts, clot in the one on the right.

B, Fetal hemorrhage into an infarct. Note the spilling of red blood cells from capillaries of necrotic villi which are branching off a cotyledon stalk at top of section just left of center. (×160.)



Figs. 8 and 9.—Old placental infarcts. Calcification of the former, liquefaction of the latter. Note faint outlines of chorionic villi at bottom of each section indicating that the lesions are true infarcts. (×160.)

somewhat different. In no case was healing by granulation tissue formation observed. There were no budding capillaries and only minimal if any fibroblastic proliferation at the margins of lesions. Old placental infarcts were characterized by calcification, when small (Fig. 8). Larger ones became calcified at the margins and liquefied in the centers (Figs. 9 and 10). Occasionally there was feeble proliferation of sickly-appearing trophoblastic cells at the margins of such lesions (Fig. 9). Small foci of old hemorrhage were often found in infarcts of this stage.

Differential Diagnosis.—

Other nodular lesions which, in certain respects, simulated placental infarcts grossly were: (1) fibrin deposits, (2) intervillous thrombi (often erroneously called intervillous hematomas), (3) cystic degeneration of decidual septa or of trophoblastic cell columns, and (4) chorioangiomas.

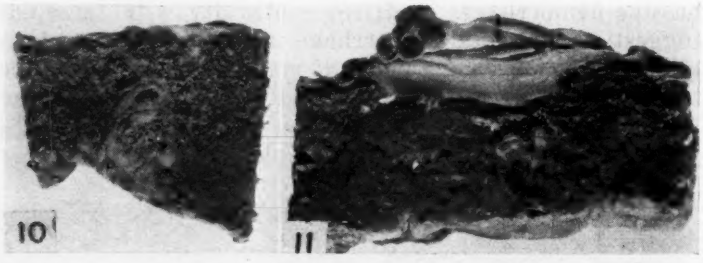


Fig. 10.—Old (gray) infarct, becoming calcified and liquefied. Note its position on the maternal aspect of the placenta.

Fig. 11.—Fibrin deposit beneath the chorionic plate at the site of cord attachment.

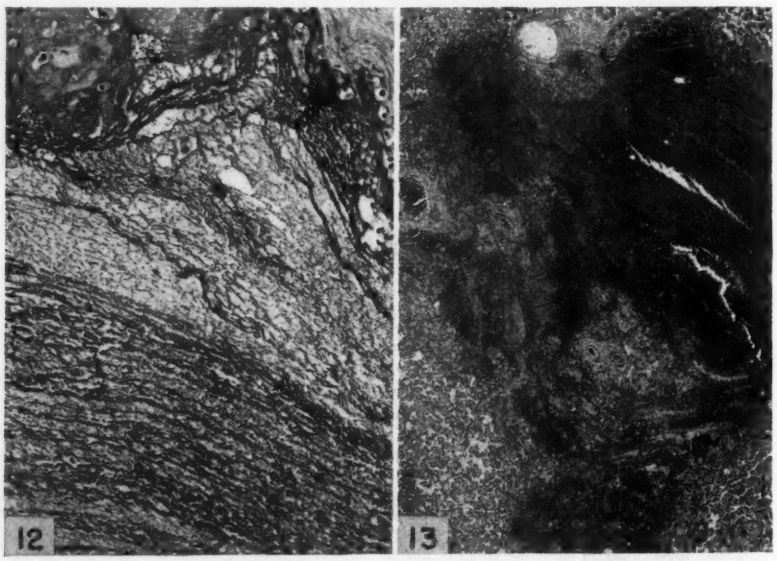


Fig. 12.—Subchorionic fibrin deposit. (×95.)

Fig. 13.—Intervillous thrombosis. (×12.)

Fibrin deposits, often confusingly called "white infarcts," occurred in many locations in the placentas but were far more frequently found as white, wedge-shaped nodules just beneath the chorionic plate (Fig. 11). There was convincing evidence that such deposits began as localized thrombosis of maternal blood, within the circulation, possibly originating at sites where small foci of degenerating trophoblast permitted maternal blood to come into contact with underlying stromal tissues, thus initiating intravascular clotting. In microscopic sections of given lesions all stages of the process were demonstrable. Following thrombosis the enmeshed red cells became hemolyzed and finally all cells disappeared leaving the fibrin, which apparently is not readily disposable in placentas. In older lesions liquefaction and calcification were occasionally seen. The laminated, nonspongy character of these lesions differentiated them grossly from true infarcts. Microscopically, the absence or sparsity of chorionic villi

made differentiation easy (Fig. 12). A few contiguous villi at the margins of the lesions occasionally showed compression ischemia.

Intervillous thrombi appeared grossly as red, laminated, nonspongy nodules of clotted blood. There was wide variation in size, shape, and location of lesions and, as described above, varying degrees of transformation into "fibrin deposits."

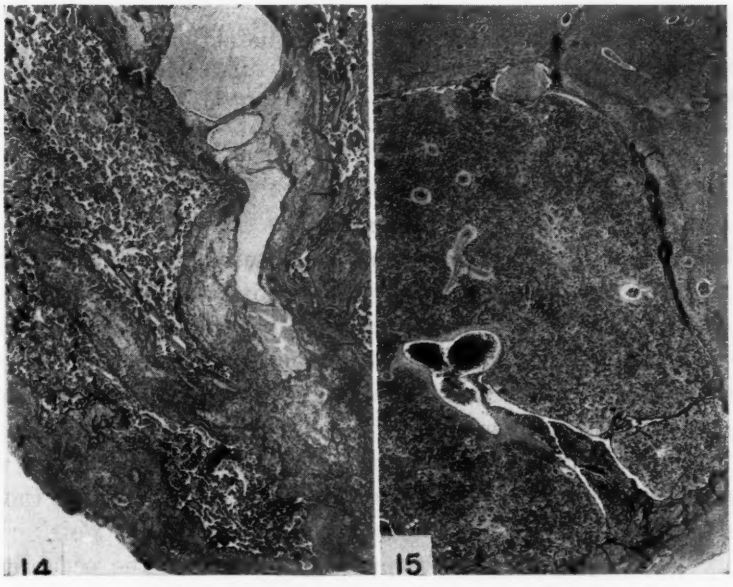


Fig. 14.—Cystic degeneration of decidual septum. Decidua basalis is on lower edge of section. (×12.)

Fig. 15.—Chorioangioma of the placenta. Decidua basalis is in the lower right corner. (×12.)

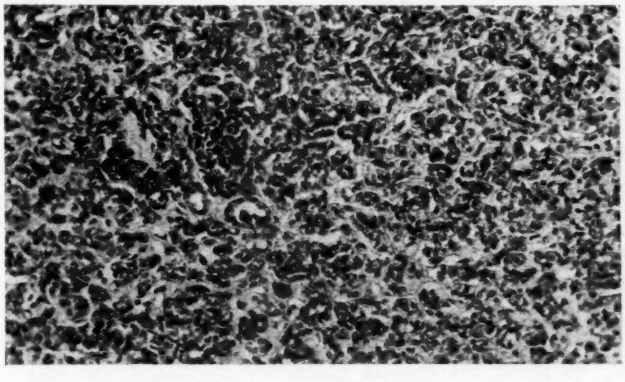


Fig. 16.—Chorioangioma of the placenta. (×160.)

However, in some cases with multiple thrombi, the uniformity in the age of lesions situated deep in the placenta suggested an etiology different from that of the so-called "white infarct." Microscopically, the laminated thrombotic character of the lesions and the absence or sparsity of villi except at the margins sharply differentiated them from infarcts (Fig. 13). Hemorrhages within infarcts usually were not finely laminated and could easily be shelled out of the lesions (Fig. 7, *A*). These were true hematomas. Occasionally similar hemorrhages, probably from the maternal circulation, were found in decidual septa. These also were true hematomas. The morphological criteria which for many years have been found useful in differentiating intravascular clotting (throm-

bosis) from extravascular clotting (hematoma) are also applicable to lesions in the placenta.

Cystic degeneration occasionally appeared grossly as nodular lesions which were in contact with the maternal surface when occurring in decidual septa. On sectioning, the homogeneous gelatinous contents of the cysts differentiated them grossly from infarcts. Microscopically, the absence of villi made differentiation easy (Fig. 14). However, this lesion was occasionally misdiagnosed grossly as an old infarct undergoing cystic liquefaction.

Chorioangioma was found only 4 times in this series and in each case was misdiagnosed "red infarct" grossly. Microscopically the lobulated character of the lesion (Fig. 15), the absence of villi (Fig. 16), and the neoplastic character of the masses of capillaries were diagnostic criteria. In one case a large portion of the nodule was infarcted, presenting an added difficulty in gross diagnosis.

Comment

It is beyond the scope of this report to discuss the various causes of placental infarcts except to state that any abnormality which separates one or more cotyledons from the maternal circulation for a prolonged period of time will probably cause infarction. There is still much to be learned concerning both the maternal and fetal blood flow through the placenta. In the present study, the finding of nodular ischemia within a few minutes after cessation of the maternal circulation to one or more cotyledons refutes the concept that the entire placenta is an undivided lake of maternal blood into which the cotyledons and villi project.

In a previous report[1] the close correlation between the occurrence of true placental infarcts and eclamptogenic toxemia was emphasized. The present report indicates the necessity for careful differentiation, often by means of microscopic sections, between true infarcts and other nodular placental lesions before the etiology and clinical significance of these conditions can be determined.

Summary

In a series of 562 entire placentas, and other specimens of gravid uteri and contents, together with material from autopsies in cases of maternal and fetal deaths, the formation, regression, and differential diagnosis of true infarcts of the placenta were studied. Diagnostic criteria were established which are comparable to those commonly used in general pathology. Accurate diagnosis, often by means of microscopic sections, is a necessity in the determination of the etiology and clinical significance of nodular placental lesions.

Acknowledgment.—The author wishes to thank Dr. Gregory T. O'Conor for his assistance during the first year of this study.

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THE NITROGLYCERIN FLICKER FUSION THRESHOLD TEST IN TOXEMIA OF PREGNANCY*

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THE ordinary 60 cycle light bulb actually flickers 60 times per second, a rate of flicker that cannot be detected by the human eye. If this rate is reduced, it will eventually be noted by every observer, usually when the flicker rate reaches about 40 per second. In reducing the flicker rate, the point at which flicker is detected by any individual, or the point at which the flickers fuse into a steady source of light, is for that person, the fusion frequency threshold for flicker, or the F.F.T. The F.F.T. of each patient remains constant under given conditions unless it is changed by the use of drugs or the development of physical or pathological entities.

Usually, vasospasm is developed in the retina as an expression of a generalized condition. Such ocular vasospasm will interfere with vision and with the ability of the subject to detect flicker. If, then, a patient is given $\frac{1}{100}$ grain nitroglycerin sublingually, the vascular spasm will be relieved, the ability to detect flicker will be improved, the F.F.T. will be raised, and the diagnosis of vasospasm becomes evident. This constitutes the Krasno-Ivy nitroglycerin F.F.T. test on which the present report is based, and the studies for which were made with the Krasno-Ivy flicker photometer.[1] Since it is believed that generalized vasomotor hypertonus is present as an integral part of toxemia of pregnancy it was felt that this test could be applied to determine the presence of this spasm in this obstetrical complication.

In a preliminary report presented by the authors before the combined meeting of the Chicago, St. Louis, and Kansas City Gynecological Societies in April, 1951,[2] the following conclusions were stated:

1. The Krasno-Ivy flicker photometer is a reliable apparatus for determining the flicker fusion threshold.
2. The nitroglycerin flicker fusion test proposed by Krasno and Ivy is a valuable aid in the detection of vascular spasm induced by toxemia of pregnancy.
3. By using this test, we have predicted the development of toxemia of pregnancy two to eight weeks before the ordinarily recognized signs and symptoms of toxemia of pregnancy appeared.
4. A positive, or abnormal, test before the advent of clinical signs of toxemia of pregnancy with adequate prophylactic therapy, may allow us to forestall the onset of the toxemia.
5. The use of the test assists in estimating the adequacy of the management of the patient.

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*Presented before the Chicago Gynecological Society, Jan. 18, 1952.

Since April, 1951, further experiments with the use of the Krasno-Ivy flicker photometer in studies upon pregnant women have confirmed the above conclusions.

Historical

The use of an apparatus for the determination of threshold for the detection of flicker is far from new. As long ago as 1855, Schafhautl[3] improvised such a machine and found variations from normal in certain pathological conditions. In the time intervening between 1855 and 1949 when Krasno and Ivy first presented their apparatus, many workers developed instruments for this purpose and there are numerous reports of these studies in the medical literature. In a monograph, Berg[4] reviews all of this work and much valuable information has been derived from his observations. Berg made his studies upon patients with cerebral injuries. He concluded that the use of the F.F.T. with Evipan supplied him with valuable data.

It is not deemed necessary, at this time, to review the method of procedure or the physiology of the phenomenon of the F.F.T. because these factors have been sufficiently presented previously by Krasno and Ivy, Berg, and the present authors. It should serve the purpose to quote a paragraph from our previous report:

"In normal subjects, the use of nitroglycerin will produce a dilatation of the arterioles and congestion of the retina of the eye with a resulting impairment of the ability to recognize flicker which is indicated by a lowered F.F.T. We shall henceforth refer to this as a negative, or normal, test. In vasospastic individuals, the retinal vessels will dilate under the influence of the nitroglycerin, the blood flow and oxygenation of the retina will be improved, and the F.F.T. will rise; in other words, the ability to recognize flicker will be improved, resulting in what we shall designate as a positive, or abnormal, test."

Material

The patient material studied was derived from several different clinics in Chicago in order to accumulate observations more rapidly. Patients attending the prenatal clinics of the Mount Sinai and Presbyterian Hospitals were tested routinely. In addition to this, private maternity patients were made available to us by the members of the attending staffs of these hospitals because they showed evidence of toxemia or of cardiovascular-renal disease or had previous histories of one of these entities. It must be emphasized that, since the patients in this latter category had been deliberately selected for this study, we can make no statistical report on the frequency of toxemia inasmuch as we have intermixed the two groups of patients tested. Added to these groups is a series of "unknowns" studied at the Cook County Hospital.

Observations

To date, we have conducted 763 tests on 353 patients. In this group 223 have constantly given normal responses. This we consider our control group. One hundred thirty patients presented abnormal or positive tests and we shall direct our attention to these (Table I).

TABLE I

Total patients tested	353
Total tests run	763
Patients with positive F.F.T.	130
Patients with negative F.F.T.	223

Table II gives the total number of positive tests, false negatives, and percentage of failure.

TABLE II

Total no. toxemia or CVR disease	114
Total no. positive patients	130
Failure or false negative	2, or 0.89%
False positive	11, or 8.4%
Failure in entire group	13, or 3.7%
Undelivered	5

In the first of these are included all the patients with pre-existing cardiovascular-renal disease, who, because of the nature of that disease, would have vascular spasm and, therefore, positive F.F.T. tests. In this group are the patients with vascular or essential hypertension, nephritis, old cardiac disease, and patients with previous pre-eclamptic toxemia who retained a positive F.F.T. between pregnancies, probably denoting permanent vascular damage. Many of these patients completed pregnancies without developing signs of specific toxemia, as such patients are prone to do. With histories of previous disease and with the positive F.F.T. these patients must be properly evaluated early in pregnancy and, if allowed to continue with their pregnancies, must be watched very carefully for signs of deterioration in the original disease or development of superimposed toxemia of pregnancy.

An interesting case study in this category is that of Mrs. K., a 26-year-old gravida ii, para i, who gave a history of having a nephrectomy in 1947 for polycystic kidneys. Her first pregnancy ended in a cesarean section in 1943 because of placenta previa. The patient was seen in the first month of pregnancy with a positive F.F.T. and no clinical signs of toxemia or renal insufficiency. At the end of the sixth month, she developed 3 plus pitting edema and 4 plus proteinuria. The F.F.T. remained positive. The patient was admitted for study and treatment. The edema and albuminuria continued, with a rise in nonprotein nitrogen to 51. She delivered a 3½ pound stillborn infant in the seventh month. The F.F.T. studies to date remain positive. The nonprotein nitrogen has dropped to 30, albuminuria and edema fluid have subsided. The blood pressure never rose above 130/80.

The second group of patients with positive tests are those who gave no history nor presented any clinical findings suggestive of old cardiovascular-renal disease or toxemia of pregnancy (Table III).

TABLE III

Toxemias predicted prior to clinical signs	57
Time of prediction	1 wk. to 6 months
Positive F.F.T.'s with no clinical signs and undelivered	5

There were 57 in this group. Of these, 52 subsequently developed signs of clinical pre-eclamptic toxemia, while 5 are as yet undelivered. The time lapse between obtaining a positive test and the appearance of signs of pre-eclampsia varied from one week to 28 weeks. Up to the present time, 11 patients without pre-existing cardiovascular-renal disease who had shown positive tests have come to delivery without showing some signs of clinical toxemia.

A good example of a patient in this group is the following:

A 17-year-old primigravida whose past history was essentially normal was found to have a positive F.F.T. in the sixth month. Blood pressure, urine, edema, and other laboratory studies were normal at that time. Approximately two months later the blood pressure was 122/96 and edema was present. She was admitted for study and was discharged in 3 days

as improved. Her F.F.T. remained positive. She was readmitted in a month with a blood pressure of 150/90, 3 plus proteinuria, and 3 plus edema. She started into labor and after the third stage developed a typical tonic and clonic convulsion. The F.F.T. was positive throughout the immediate postpartum period and reverted to normal in 6 weeks.

Forty-three patients have been tested who had already developed signs of toxemia at the time of the first test. All but one of these patients showed positive results. The one patient in this group who gave a negative, or normal, value is unexplainable. This being one of two false negative tests thus far obtained, it can be stated, statistically, that the percentage of failure from this point of view is negligible.

In this last group of patients who have been under treatment with routine orders of bed rest, phenobarbital, methionine, and the replacement of sodium by potassium in the diet, clinical improvement is paralleled by change in the F.F.T. Complete clearing of the clinical signs of toxemia with loss of weight and the re-establishment of normal fluid and electrolyte balance have been accompanied by a reversion of the F.F.T. to negative, or normal (Table IV).

TABLE IV

Toxemias with positive F.F.T., which returned to normal after treatment	22
Pseudotoxemia with negative test which remained negative after edema cleared	13

This phenomenon has occurred in 22 instances. To indicate the possible value of the test in measuring the patients' response to a management of the toxemia, we shall cite the following case history:

An 18-year-old gravida ii, para ii, with a positive F.F.T. and no clinical signs of toxemia, developed albuminuria and edema ten days following the test. She retained her positive flicker test when these signs appeared and was placed on bed rest, phenobarbital, methionine, potassium chloride, and salt-free diet for two weeks. After this period of treatment the clinical signs disappeared quickly and the flicker test returned to normal. This patient delivered spontaneously without a return of any of the signs or symptoms of toxemia and she retained her negative flicker test.

Those patients who do not show clinical improvement under "toxemia management" retain a positive F.F.T. In this group can be classified those patients who develop a negative test soon after delivery even though the toxemia prompted induction of labor. In a group of 31 postpartum patients, 12 reverted to normal tests in from one day to 10 weeks following delivery. Those who retained positive findings indefinitely post partum must be considered as having permanent residual damage as a result of toxemia.

The final class of patients that has been observed is that group in which there exists edema because of disturbance of water and electrolyte balance with no other signs of pre-eclampsia. Dieckmann and associates[5] classify these patients as having toxemia, but not pre-eclampsia. All of these cases clear up under a regimen directed toward changing the electrolyte and fluid balance. There were 13 patients in this group, all of whom had negative, or normal, F.F.T. throughout pregnancy and who developed no true signs of pre-eclamptic toxemia.

Comment

There is considerable discussion in the current medical literature concerning the F.F.T., much of it adverse. All of this work is being done by internists, chiefly cardiologists, who are dealing with groups of relatively elderly

patients with disease of the vascular tree of long standing. Toxemia patients are chiefly young women who were in good health prior to the onset of pregnancy. Many of them have negative F.F.T. tests early in pregnancy. To compare this group with elderly men having basic degenerative cardiovascular-renal disease is unfair.

Because the results obtained have been so consistently confirmative of our previous conclusions and projected ideas, it is felt that the F.F.T. nitroglycerin test, as determined by the Krasno-Ivy flicker photometer, is a valuable diagnostic and prognostic aid in the study of toxemia of pregnancy. Women who proceed through the first two-thirds of a gestation with the F.F.T. test normal or negative can be safely assured that they will probably not develop pre-eclamptic toxemia for that pregnancy. Patients presenting an abnormal or positive nitroglycerin F.F.T. test will fall into one of the following classes:

1. Patients with previously existing cardiovascular-renal disease.
2. Patients with previous toxemia of pregnancy with residual vascular damage.
3. Patients who have presently existing pre-eclamptic toxemia.
4. Patients who will develop toxemia before termination of this pregnancy.

The first group of patients discussed is that in which was predicted, by this test, the subsequent development of pre-eclamptic toxemia in the absence of any then existing clinical signs of such a toxemia. At the time of the first positive F.F.T. test there were, in those of the patients tested for these entities, no changes in the blood chemistry values and no evidence of retinal vasospasm as detectable by direct retinoscopy. Most of the patients in this group eventually, during that pregnancy developed clinical signs of toxemia. Five of the patients who did not do so are still undelivered. It is presumed that these will exhibit toxemic manifestations before delivery. From this we feel safe in stating that the F.F.T. will uncover the likelihood or predilection to toxemia in any given pregnancy before the onset of clinical signs and before such a tendency can be detected by blood chemistry or eye ground studies.

The second type of patient who can be evaluated in a rather definite manner by the F.F.T. test is that woman who develops edema without other signs of pregnancy toxemia. This is the "pseudotoxemia" of Dieckmann and collaborators. These patients have edema on the basis of abnormalities of water and electrolyte balance, and are relieved of the edema by the replacement of sodium by potassium either parenterally or orally. We, therefore, can conclude that these patients do not have potential toxemias. Dieckmann's work bears out this conclusion.

The third series to be called to your attention is that one in which true pre-eclamptic toxemia exists or develops. All of these have positive F.F.T. tests. Those who respond to "toxemia management" with restitution of the blood pressure, edema, and urinary findings to normal also show a reversion to normal in the F.F.T. test. Those who did not respond to therapy retained

positive tests. This is considered a very important signal. If a patient under toxemia treatment does not show a reversion of the F.F.T. test to normal within a relatively short time, it is concluded that she is not responding to treatment.

The fourth classification of patients considered is that which includes all women with pre-existing cardiovascular-renal disease regardless of etiology. All of these had positive F.F.T. tests. Our interest in these women is primarily aimed at determining the advisability of future pregnancy, or, if pregnant, whether the pregnancy should be interrupted. In our opinion, patients who show a positive test with history or findings of pre-existing cardiovascular-renal disease and those who retain a positive F.F.T. test indefinitely following a pre-eclamptic or eclamptogenic toxemia may be further insulting their vascular systems, possibly irreparably, by the addition of another pregnancy load to an already damaged organism. Some of these patients have normal blood pressure and negative urinary findings at the time of testing.

The final group is that one in which tests were performed post partum on patients having positive tests during the course of their pregnancies. All of the patients who showed normal tests within the first six weeks following the termination of the pregnancy can be considered as having had merely a toxemia of pregnancy. It is assumed that these women have reverted to normal with the removal of the insults provided by the pregnancy, and that they probably will never show any ill effect as a result. Future pregnancy would not be contraindicated in these patients. Those who have retained a positive test beyond the six-week period were in the true cardiovascular-renal group or in those who suffered toxemia with no previous history of disease. We believe that these latter patients have residual vascular damage from the toxemia and that, if the F.F.T. remains positive, they can be classified with the former group (Table V).

TABLE V

No. of patients having positive F.F.T. during pregnancy tested post partum	25
No. of patients having toxemia with test returning to normal	10
No. of patients having toxemia retaining positive test	3
No. of patients having C.V.R. disease retaining positive test	12

Conclusions

1. The Krasno-Ivy flicker fusion threshold nitroglycerin test is of value in the study of toxemia of pregnancy.

2. By use of this test it has been possible to predict the onset of toxemia of pregnancy before any clinical evidence of that disease becomes apparent.

3. The test has permitted the evaluation of the efficacy of treatment in toxemia of pregnancy.

4. Cardiovascular-renal disease, pseudotoxemia, and toxemia have been differentiated through the use of this test.

5. The results, as given, have made it possible to some extent to determine the advisability of future pregnancies following a previous toxemia or cardiovascular-renal disease.

The authors wish to acknowledge the aid given them by the Clinical Instruments Company of Chicago, the manufacturers of the Krasno-Ivy flicker photometer, who provided them with the instruments used for this study.

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Discussion

DR. FREDERICK J. HOFMEISTER.—All who practice obstetrics must be genuinely interested in the potential value of the flicker test in relation to this specialty. This is a must when one considers the results described in this very interesting and thorough presentation. Since the original report about one year ago, the number of patients examined has approximately been doubled as have the number of individual tests performed. The results in both series are essentially the same, excellent. How can one ignore the possibility of having at one's fingertips something which will be of assistance in preparing to combat an entity which is still considered one of the triad accounting for 85 per cent of all maternal deaths.

We are personally interested because in the five-year period from 1947 through 1951 there were 12 cases of convulsions in 328 toxic or pre-eclamptic patients among the 14,529 patients delivered at Milwaukee Hospital. We feel this is too many in spite of the fact that we are certain of the excellent prenatal care these patients have had. Is it not possible by detecting the tendency toward toxemia and instituting rigid treatment before symptoms appear that this incidence might be materially reduced Along with this, hemorrhage, and in some institutions death by shock and hemorrhage, another of the great triad, might indirectly be reduced. It is stated by Greenhill that Portes reported toxemia associated with abruptio in 91.3 per cent of their cases and Greenhill found toxemia associated in 56.6 per cent of their cases. Might we not reduce this catastrophe by the early combat of toxemia?

To be able to anticipate these conditions in advance and possibly to prevent them would be sufficient. But, in addition, to be able to determine the patient who has been previously toxic and who is potentially a future toxemia patient by virtue of retained subclinical cardiovascular-renal damages would be another great step forward. One would hesitate to advise pregnancy knowing that the patient would become toxic and probably accumulate further cardiovascular-renal damage. When one considers this entire picture it seems almost too good to be true.

Does this Flicker Photometer test fulfill the criteria of a practical laboratory procedure? In order to evaluate this test personally, a much greater time is required than that which has elapsed. Naturally we have had insufficient time to collect an adequate series, and many more tests must be performed before we will be certain of our accuracy. We determined to assemble as quickly as possible patients demonstrating the various complications for which this test is of value.

6 known toxic patients were found to be Flicker positive
1 patient with edema was negative. This should indicate that she will not become toxic. She will be followed to delivery.
3 patients known to be normal had negative tests.
2 postpartum patients were both pre-eclamptic before delivery. One was negative on the ninth day, one was positive on the sixth day.
1 patient, known to have cardiovascular-renal disease with albuminuria and hypertension in excess of 200, in her last month of gestation, was Flicker negative.

Two of the patients had headaches sufficiently severe to arouse complaint.

Generally speaking, this very insufficient number of cases gives results which coincide with the results obtained by the essayists. They had two false negatives, one in a known

toxic patient. We had a false negative in a known cardiovascular-renal patient. One certainly does not make a bushel, but having been impressed with this test as a reliable indicator of residual damage, we would hesitate to prognosticate, knowing that in these limited series there were instances of nonconformity to the rule. The two instances of false positives could result in little damage during the course of pregnancy except that they might result in overcaution and restriction if accepted on face value. However, in the hands of the unscrupulous and the easily impressed it is conceivable that unnecessary cesarean section or interruption of pregnancy could be the result.

The other conceivable complication of a false positive test could be in the nonpregnant who would erroneously be advised against conception. I realize that these speculations might be far fetched when professional people of the caliber gathered here are considered, but we cannot ignore what has happened and is happening with the valuable Rh and Papanicolaou tests when proper clinical judgment and honesty are lacking. This test will be in the hands of all practitioners since it conforms to the criteria necessary for a practical test. It is easily performed, it can be performed for little cost, the apparatus is not too expensive, and it has great flexibility since it can be performed in the office as well as in the hospital.

There are several other questions that must be answered.

What is the authors' opinion concerning the unmeasurable human element of error? Both the operator and the patient tested can err in judgment. This could be a big factor. Dr. F. D. Murphy, an outstanding authority in the field of heart disease and nephritis, in a personal interview stated that he was impressed in the 100 tests they performed by two factors:

1. The severe headache which frequently interfered with the patient's ability to concentrate on the light beam.
2. The element of human error in judgment.

We agree that he is dealing with a different type of patient, and in a different age group, but technically the problems are the same. Has the incidence of headache been a factor with the essayist?

Fox and Wright in the September, 1951, issue of *Circulation* state that their results indicate that the Flicker test in itself is not a sufficiently accurate and objective method of demonstrating the presence or absence of vasospasm. Actually it is this that the test depends upon in the toxic patient.

We believe this test may have a distinct value in our field if additional series of tests confirm the excellent work done here. However, more cases must be accumulated, the pharmacology of nitroglycerin must be clarified, and caution must be exercised in the introduction of this test to the profession lest it be wrongly interpreted and used as were the Rh and Papanicolaou tests. We have the fever now and it would be difficult to take the apparatus away from the resident who has expressed a desire to continue the observations.

DR. LESTER D. ODELL.—Anything which serves to differentiate the patient with toxemia, or the patient destined to develop toxemia, from the nontoxic patient is certainly worthy of complete investigation. As all of us know, the cost of prenatal and hospital care is ever mounting; if a simple screening test is found, much can be done to decrease cost and improve mortality figures by segregating the potentially dangerous cases. The patient safe from toxemia certainly would require fewer prenatal visits late in pregnancy. Although the response by our profession to the flicker fusion test may not be entirely favorable at the present time, all the essayists ask, as I understand it, is that we try the test and see if we obtain as favorable results as they have.

An ideal test for toxemia of pregnancy should probably possess several characteristics. It should be specific, it should warn the doctor of an impending toxemia, it should distinguish pre-eclampsia from essential hypertension, it should be of prognostic value, and the method of analysis should be relatively easy and accurate. As we know, the candidates which have been proposed as "the test" are legion, and the majority of these tests have been forgotten. Whether the flicker fusion test will remain or not will be determined only by time. My own

contact with the test leads me to believe that it might be one of the better semilaboratory guides available at the present time. The technique is well within the scope of the practicing physician, it apparently has a higher specificity than other tests with which I am in contact, and the essayists feel that it is of prognostic value and that it warns of impending toxemia. In spite of the good results observed in this study I still believe that the best prognostic guide lies in clinical judgment and that the rate of weight gain tells the practicing physician much as to impending toxemia.

According to a previous publication by the essayists the flicker fusion measures the presence of vasospasm or vasomotor hypertonus in the ocular fundus. It has been suggested by many authors that toxemia is essentially a vascular disease. Hertig has suggested that the common denominator underlying the varied pathology of eclampsia is vascular spasm. Furthermore, one sees the obvious clinical fact that hypertension itself must rely on some degree of vasospasm, and sometimes one may even see constricted vessels in the eye grounds. There are, however, some observations which would lead us to believe that vasospasm is not present in all cases of toxemia and that it may be present in some nontoxic patients. These points are as follows: eclampsia has been observed in patients with relatively normal blood pressures; the renal blood flow as determined by Diodrast or para-amino-hippuric acid is reported as normal in cases of eclampsia and it is doubtful if the kidney is ischemic from spasm; tests which measure the degree of vasospasm such as the cold pressor and Pituitrin tests may give false positive responses in nontoxic patients or false negative reactions in toxic patients; most authorities agree that water retention precedes the development of hypertension (spasm) and spasm therefore may represent a late manifestation of the disease; direct observation of the vascular bed would indicate that although dramatic changes occur in the venule and capillary bed during eclampsia, no specific change is found in these vessels during nonconvulsive toxemia which cannot be found in other unrelated processes (infection, trauma, normal puerperium). It might be that we should look elsewhere for the pathologic lesion of toxemia.

Dr. Long and I have observed that a positive flicker fusion test can be obtained on a normal patient during the cold pressor test. Similarly, during labor a false positive reaction occurs. Selye has proposed that toxemia is part of a general adaptation syndrome, of a response to stress. Whether this theory is just another band wagon or not I do not know, but I think it is a line worthy of investigation. The flicker fusion test may only measure the response of the body to stress since positive reactions have been reported in such related conditions as fatigue, anoxia, anxiety, and cardiovascular disease, as well as during the cold test and during labor.

DR. EDWARD ALLEN.—I have been interested in this test because much of the work has been done in the Central Free Dispensary of the Presbyterian Hospital. I have consistently insisted on controls, the importance of which the previous discussors have brought out. I am interested to hear that false results have arisen. I think the increase in these false results indicates that the workers are endeavoring in different ways to check their results and that they have been able to follow these patients longer and have brought out false positives and false negatives. I think the false positives are much more important. I believe we cannot give patients too great care when we are considering the subject of toxemia. The false negatives are not important because they did not eventuate into serious disease.

A great many of these tests have been performed on patients in whom the diagnosis was known before the test was begun. If we think of this test in terms of scientific information, the final answer may be in the examination of large numbers of obstetric patients without knowing anything about the patient. If these results are anywhere near as good as this report would indicate, the test would be a great addition to our armamentarium in the diagnosis and perhaps in the treatment of toxemia.

We have wondered if, in addition to changes in the central nervous system, disturbances in gland balance including the thyroid, which occur in all pregnancies, may not be contributory factors. Disturbances in gland function have been suggested as possible etiological factors in toxemias.

DR. KLAWANS (Closing).—Since our first report was presented in April, 1951, we have had many inquiries from within the profession. We had one communication from Philadelphia in which the writer informed us that he was doing work with the test and was obtaining interesting results.

Professor Halstead's discussion was the discussion of a pure scientist who is apparently endeavoring to coordinate pure science with clinical research. I am picking a bone with Professor Halstead in his feeling concerning the great value of the intensity of the light. That to us in unimportant because each test, as we conducted it, is a test in itself. In each patient is established a new level and we are merely carrying out a test which is designed to show the effect of nitroglycerin on this patient's vasospastic condition or on her blood vessels. Therefore, whether the light is one year old or ten years old, each test establishes its own base line, and therefore the base line established even two weeks ago is unimportant.

Dr. Hofmeister made some interesting comments. As far as the human element in handling the machine is concerned, this factor will be eventually eliminated by the fact that the manufacturer is working on a machine that will be completely controlled by the patient.

We have not seen any headaches. We have seen patients who are light headed but they did not have really annoying headaches.

Dr. Odell points to the weight gain as the most important factor in the development of toxemia. We have been able to pick out patients who gained weight early as a result of electrolyte imbalance as compared to those who gain weight because of toxemia. Unfortunately, perhaps we have accepted as toxemia, cases which should not have been so accepted. Krasno and Ivy and their co-workers felt that this test is testing the vasomotor system. Halstead along with the neurologists believes that this test has more to do with brain function than it has to do with actual vascular change or vascular spasticity. Berg, in his monograph in which he studied patients with cerebral damage, felt that the process of disturbances in the flicker fusion threshold was a process of fibrillation of the brain fibers rather than a change in the vascular system. We have accepted Krasno and Ivy's contention that the test is based on vasospasm. Second, we have also accepted that the vasomotor system is the primary element in the production of toxemia of pregnancy. We may have been very naïve in accepting this as a primary basic fact.

I wish to take this opportunity on behalf of my colleagues to thank Dr. Allen for making the Presbyterian Hospital patients available to us and for his advice, encouragement, and backing. Without his help we would not have been able to carry on this work.

HYSTERECTOMY FOR BENIGN PELVIC CONDITIONS*

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SURGICAL extirpation of the nonmalignant uterus has been the subject of voluminous study in recent years. Contentions have been advanced as to the advantages of one type of procedure over another on the basis of lessened morbidity, mortality, fewer hospital days, patient comfort, etc. In many instances these differences seem academic, and it may well be that a definite hazard exists in attempting to stereotype the manner of treatment in any given case. The patient who suffers morbidity after vaginal hysterectomy might well have escaped the complication by abdominal surgery, but the vaginal procedure was best suited to her needs and physical status. Again, the persistence in removing the cervix in all cases of abdominal operation, in the face of extensive residues of infection or induration, not only accomplishes little but suggests a lack of judgment in the operator. The present survey was undertaken to evaluate a group of similar cases from a single service, with the view of demonstrating any marked disparity in results.

Material Studied

In the period from 1940 to 1951, inclusive, a total of 640 hysterectomies were performed in which the preoperative diagnosis was of a nonmalignant character. These operations were all performed on one service (service of Schmitz, Towne, and Smith), utilizing the same operative technique and subjected to the same preoperative and postoperative care. This surgical era saw the advent of antibiotics, early ambulation, wartime crowding of hospitals, and the free use of whole-blood transfusions. These factors, we feel, exerted no little influence on the end results which were obtained. Table I demonstrates that the bulk of cases were approximately divided between abdominal and vaginal procedures, offering a unique opportunity for comparison.

TABLE I

OPERATION	NUMBER OF CASES	PERCENTAGE
Total abdominal	310	48.59
Subtotal abdominal	43	6.59
Vaginal	287	44.82
Total	640	100.00

Table II discloses that the majority of patients, as might be expected, were found in the fourth to the sixth decade of life. The older patient was more frequently subjected to the vaginal procedure, both by virtue of the work indicated to be done and the minimal trauma in the presence of cardiovascular renal disease and senile debilities.

*Presented before the Chicago Gynecological Society, March 21, 1952.

TABLE II. AGE DISTRIBUTION

AGE GROUP (YEARS)	TOTAL ABDOMINAL HYSTERECTOMY	VAGINAL	SUBTOTAL
20-30	15	–	2
31-40	96	48	19
41-50	135	105	16
51-60	45	87	1
61-70	12	34	2
71-80	1	1	1
Unknown	6	12	2
Total	310	287	43

Tables III, IV, and V show the extent of the surgery performed. All adjunctive procedures such as appendectomy are performed only on indication. The use of the Pfannenstiel incision discloses the not infrequent existence of fascial defects at the lateral angles of the wound and their repair is effected at the time of closure.

TABLE III. TOTAL ABDOMINAL HYSTERECTOMY

OPERATION	NUMBER OF CASES
Hysterectomy	80
Hysterectomy and bilateral salpingo-oophorectomy	106
Hysterectomy and unilateral salpingo-oophorectomy	82
Hysterectomy and appendectomy	33
Hysterectomy and herniotomy	7
Hysterectomy and vaginal plastic	2
Total	310

TABLE IV. SUBTOTAL HYSTERECTOMY

OPERATION	NUMBER OF CASES
Hysterectomy	10
Hysterectomy and bilateral salpingo-oophorectomy	16
Hysterectomy and unilateral salpingo-oophorectomy	5
Hysterectomy and appendectomy	10
Hysterectomy and cholecystectomy	1
Hysterectomy and bilateral salpingo-oophorectomy and colostomy	1
Total	43

TABLE V. VAGINAL HYSTERECTOMY

OPERATION	NUMBER OF CASES
Hysterectomy	63
Hysterectomy, anterior colporrhaphy, and perineorrhaphy	176
Hysterectomy and perineorrhaphy	18
Hysterectomy and anterior colporrhaphy	4
Hysterectomy, anterior colporrhaphy, perineorrhaphy, and bilateral salpingo-oophorectomy	7
Hysterectomy and unilateral salpingo-oophorectomy	9
Hysterectomy and bilateral salpingo-oophorectomy	2
Hysterectomy and vaginal obliteration	3
Hysterectomy and ovarian cystectomy	5
Total	287

Pathology and Symptomatology

A study of the surgical specimens has been both thought provoking and instructive. As can be seen, myomas were found in 60.7 per cent of cases and formed the primary surgical indication in all three groups. What is more im-

TABLE VI. PATHOLOGY OF ORGANS REMOVED VAGINALLY

Myomas	111
Chronic cervicitis	105
Adenomyosis	41
Polyps	16
Fibrosis uteri	13
Leukoplakic cervicitis	14
No pathology	5
Hyperplastic endometritis	4
Adenoacanthoma	4
Chronic salpingitis	4
Simple ovarian cyst	4
Serous cystadenoma	2
Endometriosis	2
Dermoids	2
Carcinoma of the cervix	1
Retained secundines	1

TABLE VII. PATHOLOGY OF ORGANS REMOVED IN TOTAL ABDOMINAL HYSTERECTOMY

Myomas	244
Chronic cervicitis	42
Endometriosis	29
Simple ovarian cysts	43
Salpingitis	21
Benign ovarian cystomas	16
Adenomyosis	20
Polyps	12
Tuberculous salpingitis	4
Malignant ovarian cystadenoma	3
Sarcoma	1
Adenocarcinoma	1
Carcinoma of the cervix	1
Fibroma of the ovary	1
Dermoids	3
Brenner tumor	1
Cystadenomas	2

TABLE VIII. PATHOLOGY OF ORGANS REMOVED BY SUBTOTAL PROCEDURE

Myomas	34
Salpingitis	12
Endometriosis	5
Adenomyosis	2
Endometrial carcinoma, Group I	1
Endometrial polyp	1
Carcinoma of rectosigmoid	1

TABLE IX. SYMPTOMATOLOGY

SYMPTOM	NUMBER OF CASES	PERCENTAGE
Bleeding	288	45.00
Pain	197	30.78
Urinary symptoms	162	25.31
Prolapse	124	19.37
Dysmenorrhea	98	15.31
Backache	84	13.12
Abdominal mass	78	13.00
Asymptomatic	58	12.18
Secondary (fatigue, dizzy spells, edema, etc.)	133	20.78

portant is the disclosure of the presence of malignancy in 13 instances. We employ preoperative curettage routinely in all cases other than those that have been under observation for some time. The diagnosis of malignancy was determined microscopically in all instances and represented, for the most part, degenerative changes. These findings serve to emphasize the cryptic nature of ovarian carcinoma and early endometrial carcinoma.

The various pathological conditions produced a symptomatology which is classical in the sense that it follows the expected clinical picture. The principal number of patients sought medical aid for actual distress or for the more dramatic symptom of bleeding. In only 58 instances was the pathology discovered through routine physical examination. Included in the group of cases of bleeding were all those patients who had intermenstrual bleeding as well as any derangement of the menstrual habit. The principal type of bleeding was a prolongation or exaggeration of menstrual flow.

TABLE X. MORBIDITY

CAUSE	VAGINAL HYSTERECTOMY	TOTAL ABDOMINAL HYSTERECTOMY	SUBTOTAL
Cystitis	44	26	2
Pyelitis	11	7	1
Pneumonitis	4	7	1
Upper respiratory infection	5	6	1
Dehydration	3	6	1
Undetermined	6	8	1
Wound infection	–	6	2
Pelvic abscess	2	–	–
Thrombophlebitis	2	2	–
Retained sponge	1	–	–
Peritonitis	–	1	–
Enteritis	–	1	–
Total	78	70	9
Morbidity percentage	25.16	24.42	20.93

TABLE XI. HOSPITAL DAYS

DAYS	10	10-15	16-20	21-25	25
Total abdominal hysterectomy	95	169	24	13	9
Vaginal	60	170	36	6	5
Subtotal	7	30	2	2	2

TABLE XII. SURGICAL COMPLICATIONS

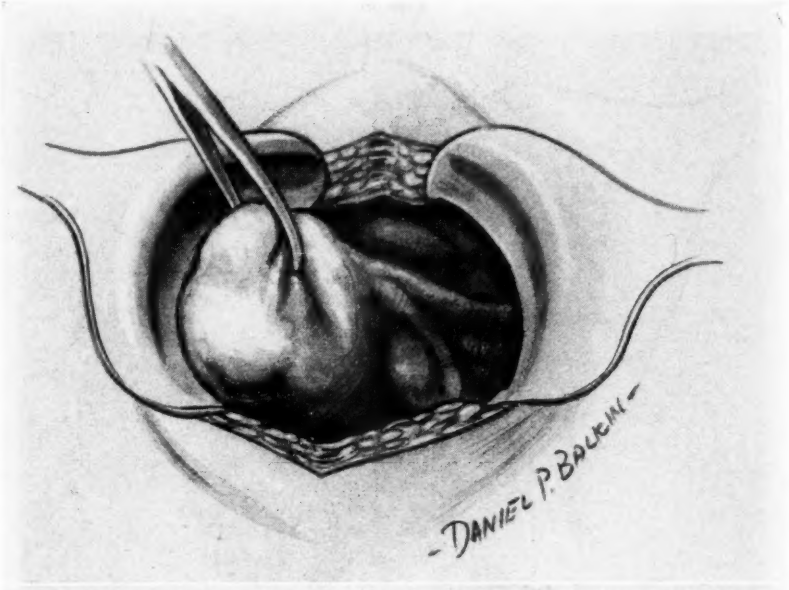
SITE	VAGINAL	TOTAL ABDOMINAL HYSTERECTOMY	SUBTOTAL
Ureter	1	1	–
Bladder	3	1	–
Bowel	–	1	1
Evisceration	–	1	1
Total	4	4	2

Results

The morbidity rate in the 640 cases was 24.53 per cent as determined by the accepted criteria for obstetrical morbidity. We are in agreement with Jones,[1] Edwards,[2] Weir,[3] and others that the morbidity figures for surgical procedures suffer in comparison by these rigid criteria and that some standardized revision is in order. The largest incidence of morbid cases were those associated with the urinary tract, while the respiratory system accounted for

the second greatest incidence. The significance of the morbidity is reflected in an analysis of the lapsed hospital days. Despite the high morbidity rates the vast majority of the patients were not hospitalized beyond average normal periods. If we accepted the normal hospital period as 14 days for abdominal

Fig. 1.



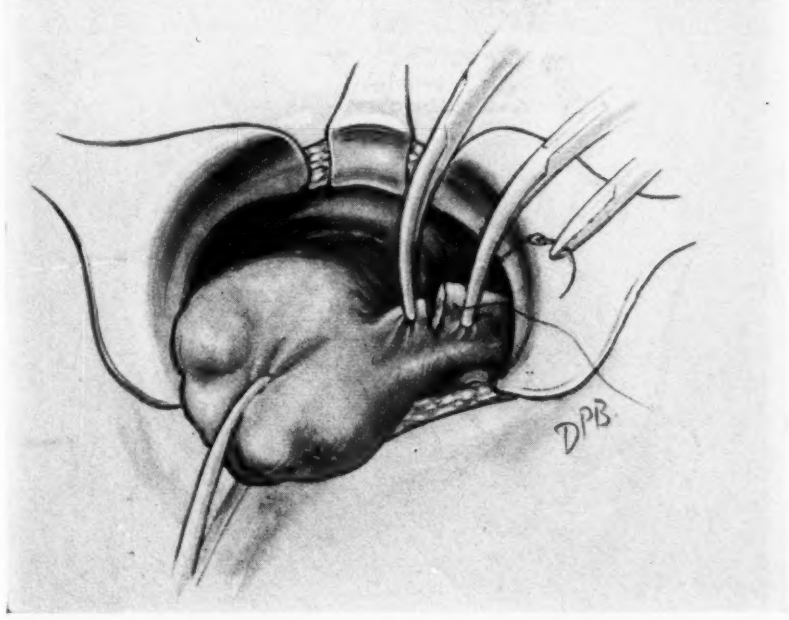


Fig. 2.

and 12 days for vaginal hysterectomy, as suggested by Miller,[4] 83 per cent of our patients were discharged within satisfactory limits. Two patients succumbed as a result of their surgery, a mortality rate of 0.30 per cent. One of the deaths followed a supracervical hysterectomy; the patient died on the

second postoperative day, from what was apparently acute renal failure. No autopsy was permitted. The second death was that of a patient who had a vaginal hysterectomy and who died on the eighth postoperative day from a retroperitoneal abscess and bronchopneumonia.

The surgical complications are shown in Table XII.

Fig. 3.

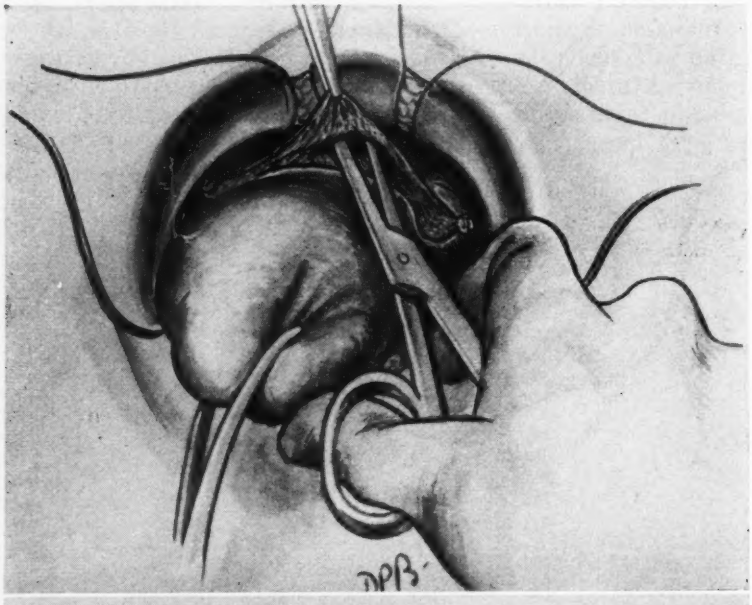
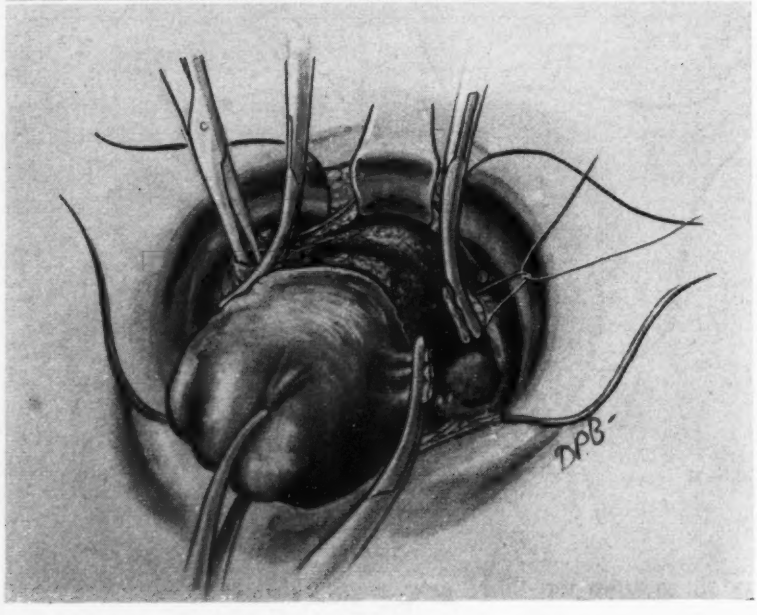


Fig. 4.

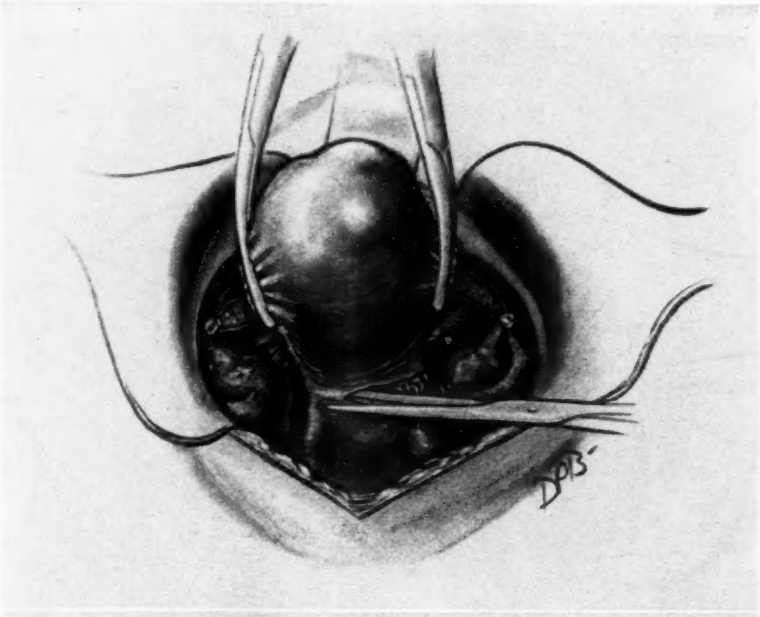


Comment

While the number of subtotal hysterectomies in our series is too small to be statistically significant, the general pattern of morbidity distribution is

that encountered in most reports, i.e., the greatest morbidity occurs in vaginal hysterectomy and is followed by that in total abdominal hysterectomy. The only explanation for the comparatively low morbidity rates that we can offer is the fact that the patients were all on the private service and were subjected to essentially identical techniques. Free use of antibiotics and supportive ad-

Fig. 5.



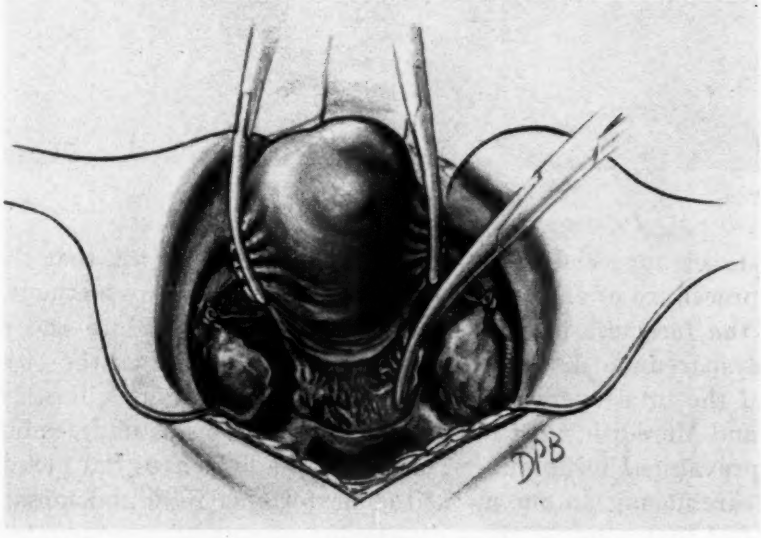


Fig. 6.

juncts possibly held many cases below a morbidity status. Curtis and Huffman[5] have reported a decreased morbidity in a series of cases which they ascribe to improved surgical care.

Our figures demonstrate only a minor variation between the morbidity rates of total abdominal and of vaginal hysterectomy, while the rate in the subtotal operation is appreciably lower. However, the death in the subtotal group gives that procedure a mortality rate of 2.3 per cent. This rather paradoxical situation is also demonstrated in the reports of Danforth[6] and Miller.[4] Schmitz,[7] in a study of 3,129 supracervical hysterectomies for myomas, showed the mortality rate to be 2.1 per cent and that the rates reported by six other authors ranged from 1.2 per cent to 2.7 per cent. A review of several representative reports[3, 8, 9, 10] shows the mortality in both the vaginal and total

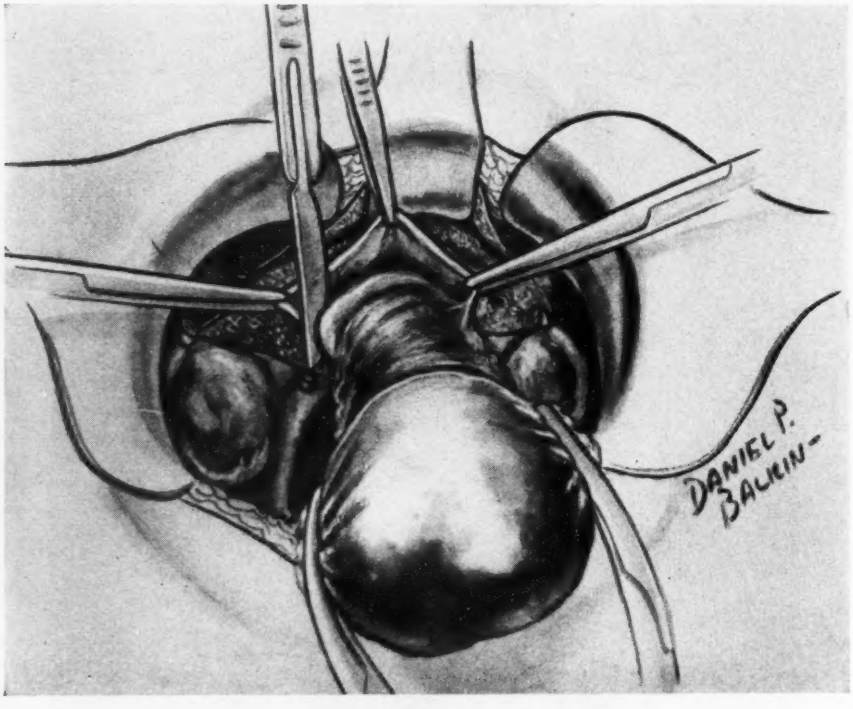


Fig. 7.

operation to be appreciably less. It would seem, therefore, that the decision as to the procedure of choice would rest between these two methods. Frank[11] is one of the foremost proponents of the subtotal procedure and cites pain, dysuria, dyspareunia, dryness, scarring, and shortening as the objectionable features of the total operation. However, Crawford and Collins,[12] as well as Aldridge and Meredith,[13] list many of these symptoms as undesirable sequelae of the supravaginal technique. These are in addition to the definite hazard of stump carcinoma. In our method of performing total abdominal hysterectomy, we feel that many of these distressing complaints are obviated by satisfactory support of the vaginal vault. By approximating the round to the cardinal ligaments on each side, a firm, fan-shaped support is obtained when healing is completed which suspends the angles of the vault from the lateral pelvic wall. The important features of the technique are demonstrated in the

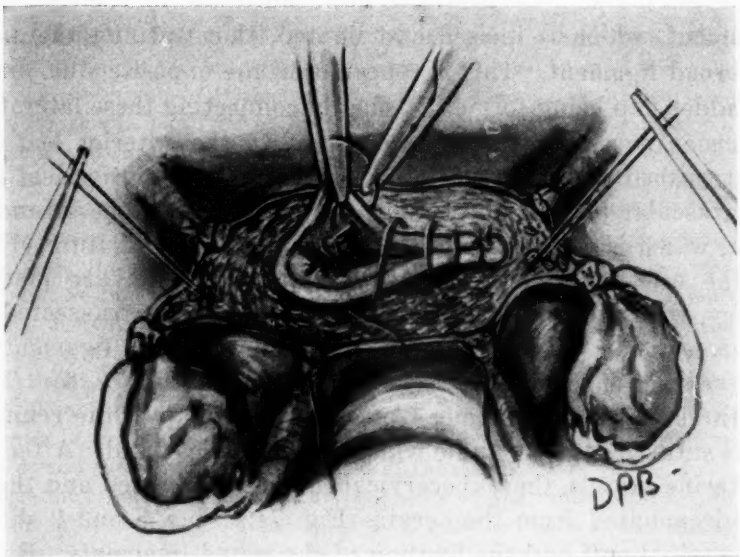


Fig. 8.

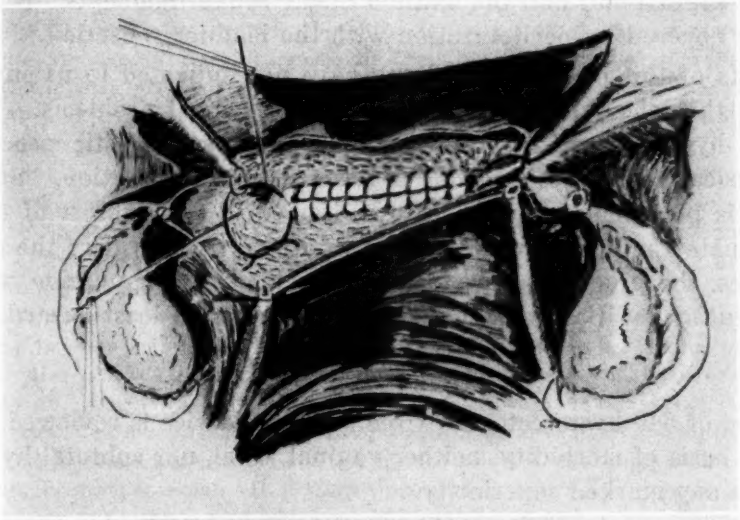


Fig. 9.

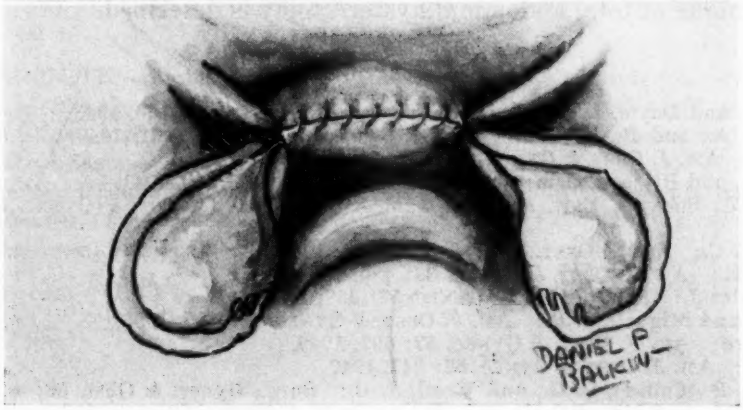


Fig. 10.

illustrations. Figs. 1 and 2 demonstrate how contralateral traction exposes the round ligament, which is incised and ligated, thus opening the anterior sheath of the broad ligament. This is repeated on the opposite side, and Fig. 3 shows the bladder flap being formed by simply connecting these lateral openings by an incision across the uterine body. With the anterior leaf of the broad ligament pushed down with the bladder flap, the posterior leaf is perforated in its avascular portion and clamps are placed across the infundibulopelvic ligament, which is then cut and secured by a transfixed suture (Fig. 4). By drawing the uterus forward, the uterosacral ligaments are placed on tension and they, with the posterior peritoneal reflection, are transected. The uterus is now freed from all attachments except the cardinal ligaments with their enclosed vessels, which are now clamped and ligated (Fig. 6). The suture securing these vessels is left long to receive the stump of the round ligament when it is sutured into the angle when the vagina is closed. After hemostasis of the uterine vessels, the pubocervical fascia is mobilized and the vaginal reflection circumcised from the cervix (Fig. 7). Figs. 8 and 9 show the closure of the vaginal cuff and the fixation of the round ligaments. Raw surfaces are then covered by peritonization with the bladder reflection.

The results of this eleven-year survey have not indicated to us any need for change in the selection of procedure for our surgical problems. We reserve vaginal hysterectomy for those patients requiring plastic procedures or whose physical status recommends a less traumatic operation. Subtotal hysterectomy is performed only when it is deemed in the interest of the patient to terminate the operation or unwise to attempt removal of the cervix. In all instances, the procedure selected is that which, in our opinion, will relieve the patient's condition with the greatest facility and least hazard.

Conclusions

1. A series of 640 hysterectomies from a single service is reviewed.
2. On the basis of morbidity, neither vaginal, total, nor subtotal hysterectomy possesses any marked superiority.
3. A technique of total abdominal hysterectomy is described.

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55 East Washington Street

Discussion

DR. JOHN W. HUFFMAN.—Dr. Smith has presented an interesting and well-organized review of 640 hysterectomies. He has re-emphasized the many problems which arise in the performance of what is probably the commonest surgical procedure performed.

Dr. Smith can be proud of his statistics and a mortality rate of 0.3 per cent.

I hope the time has come when we can all agree with the essayist's thesis that the procedure to be selected is the one which will, in the operator's opinion, relieve the patient's condition with the greatest facility and the least hazard. There should be no argument among us as to which is the preferable route—supracervical, total, or vaginal hysterectomy, unless we wish to discuss their relative indications in a specific case. Every gynecologist is, or should be, adept in the technical performance of both the vaginal and abdominal procedures. His choice of route varies with his training, his experience, and, above all else, with his personal impression of the patient's problem.

Dr. Smith rightfully emphasized the importance of supporting the vaginal vault in total abdominal hysterectomy. I think most of us will agree that the symptoms of pain and dysuria, dyspareunia, etc., are not necessarily accompaniments of removal of the entire uterus and should not follow excision of the cervix.

Some may take exception to his emphasis on the importance of the round ligaments in support of the vaginal vault. I think it has been shown that the transverse cervical ligaments which attach the lower portion of the corpus, cervix, and the upper portion of the vagina to the fascia covering the obturator muscle and superior surface of the pelvic diaphragm are the principal supports of the uterus. Logically, therefore, they are the principal supports of the vaginal vault after the uterus has been removed. He accomplished this as demonstrated in his technique by bringing the cardinal ligament to the vaginal vault with the round ligament.

Dr. Smith also discusses briefly the cases in which malignancy was found after a preoperative diagnosis of a benign condition. This problem is one which confronts all of us. He mentioned, and I wish to re-emphasize, the necessity for curettage preceding vaginal hysterectomy. I might also emphasize the value of opening and inspecting all specimens in the operating room immediately after their removal.

Quite a few of us, I suspect, will extend the essayist's indications for vaginal hysterectomy beyond that for "those patients requiring plastic procedures or whose physical states require a less traumatic operation." Many operators will perform a vaginal hysterectomy on women who, although without notable vaginal relaxation, have an adequate vaginal canal and symptomatic uterine or small adnexal tumors which are almost certainly benign and mobile. Discussions concerning the relative merits of abdominal and vaginal hysterectomy are perennial. It is unfortunate that the two procedures have, in some instances, been put upon a competitive basis because each has its indications and contraindications.

DR. SMITH (Closing).—In regard to Dr. Huffman's discussion, one point we may consider is that there might be extenuating circumstances if such could be considered with regard to these malignant cases. In five instances the malignancies were represented by degenerative changes of a previously existing benign condition. All of them were, however, confirmed by microscopic analysis. In that group of 13 patients there were the expected number of recurrences of the malignant disease, the patients eventually succumbing to their complications.

PREMATURE INFANT MORTALITY*

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(From the Department of Obstetrics and Gynecology, the Evanston Hospital, Northwestern University Medical School)

PERIODIC surveys of hospital clinical records may serve as valuable reviews of the results of our day-to-day practices. They may indicate whether innovations represent real or only fancied improvements. Such studies when applied to the problems of the premature infant should be of interest to both obstetricians and pediatricians because of the dual responsibility involved, and because of the continued greater wastage of these infants.

Material

The premature neonatal mortality at the Evanston Hospital for the years 1929 through 1938 has been detailed in a previous publication.[1] A second ten-year series encompassing the years 1941 through 1950 is herewith presented for comparison.

Premature live births of infants weighing less than 2,500 grams comprised 5.45 per cent of 8,306 live births in the first series, but accounted for 65 per cent of the gross neonatal mortalities of 174. In the second series, premature live births have been 5.9 per cent of 13,819 live births and have accounted for 53 per cent of the gross neonatal mortality of 319. Multiple births of infants of premature weight had not been excluded from the first series, and were, therefore, included in the present study in order that the comparison might be more equal. They account for 16 per cent of the 825 infants in the second series. Both series are composed of white infants only and represent a suburban population group in which maternal nutrition should be generally adequate, and the prenatal supervision thorough.

From the disproportionate share of neonatal deaths occurring in the premature group, it is again evident that any significant steps in reducing prematurity itself, or in lessening the neonatal mortality of prematures would materially reduce over-all fetal losses.

The problems of prematurity have received much attention from both obstetricians and pediatricians in the past decade as evidenced by an extensive literature. The statistical study by Peckham[3] reporting a forty-year series of prematures at Johns Hopkins has been augmented by such studies as Tyson's[4] fifteen-year study of prematurity in Philadelphia, and the Cook County Hospital report by Plattner, Stein, and Gerber.[5] The conduct of premature labor has been reviewed by many with varied recommendations. In general, most writers agree that analgesic drugs should be minimal in dosage, if employed at all, that a precipitous first stage is to be avoided, that episiotomy should be liberal, and that the delivery itself should be accomplished

*Presented before the Chicago Gynecological Society, Feb. 15, 1952.

with the least possible trauma to the infant under circumstances producing the least degree of anoxia.[8, 9, 12] The postnatal care of the infant should include adequate oxygen and an incubator, preferably in a special premature unit.[7] Masters and Ross,[11] as well as many others, have extolled the protective value to the infant of conduction anesthesia instituted relatively early in the first stage, reporting a halving of the premature neonatal mortality rate in a series of 244 infants. Potter[13] has elucidated the importance of resorption atelectasis as a cause of premature neonatal mortality and others have reported similar findings.[14, 15] The very recent blood oxygen saturation studies of Taylor, Scott, and Govan[17] with their excellent mortality figures have highlighted further the importance of fetal anoxia as a cause of death.

Grouping

Infants have been divided again into 500 gram weight groups as follows with the indicated percentage spread for the two series:

	1929-1938	1941-1950
Under 1,000 grams	7.4%	6.7%
1,000-1,500 grams	8.5%	10.8%
1,501-2,000 grams	20.1%	16.7%
2,001-2,500 grams	64.0%	65.8%

Fig. 1 portrays the relation of birth weight to infant mortality and shows the comparative rates for the two series. A slight decrease in mortality rates is evident in all weight groups, but is most pronounced in the 1,501 to 2,000 gram group. This lowering of premature neonatal mortality despite a slight rise in the rate of premature live births will be analyzed by weight groups and by factors thought to influence mortality, as in the first study.

Figure 1. BIRTH WEIGHT AND PREMATURE NEONATAL MORTALITY.

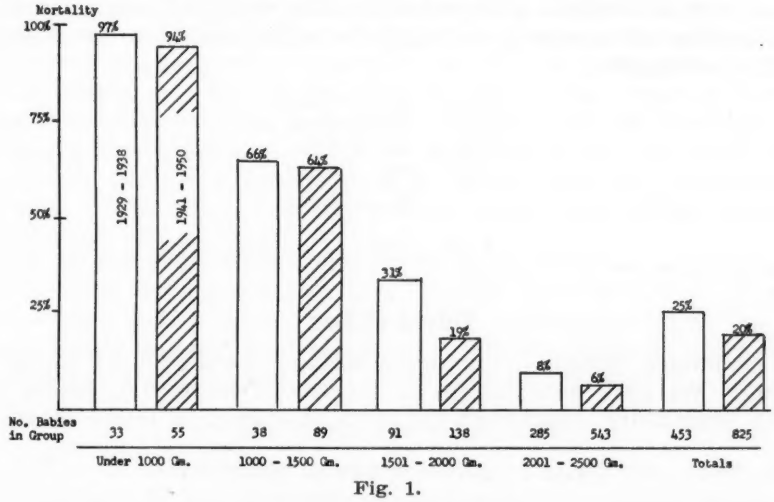

Fig. 1.

Length of Gestation

It was noted in the first study that the mortality curves for weight and estimated intrauterine age were nearly parallel. A similar concurrence was noted early in this series. As intrauterine age cannot always be determined accurately, we have again accepted weight as the most reliable single factor in determining prematurity. No further attempt will be made in this series to present mortality in terms of the length of gestation.

Parity

In the first study, the premature neonatal mortality was essentially the same for primiparas as for multiparas. It was considered that this analysis did not require repetition.

Method of Analysis

In any consideration of premature infant mortality, unless precisely similar weight groups may be compared, a correction must be made to eliminate the weight factor in the study of other factors. It is evident that a series drawn largely from the smaller weight groups will have a much higher mortality rate than would a series drawn from the larger weight groups.

To eliminate the effect of this variable spread of infant weight in consideration of the subsequent factors, we have employed again the method of weighted averages to obtain an expected mortality for each separate factor under consideration as recommended by Breese.[2] This calculation establishes a par value for the particular group of infants under study. The hazard or greater safety of the factor thus considered will be apparent as the true mortality exceeds or becomes less than the expected mortality. The true mortality of each factor may then be compared with its own expected mortality rather than an attempt made to compare the true mortalities of what may be dissimilar groups of infants. To emphasize this comparison between true and expected mortalities, we have added to each table a column labeled Deviation (Dev.) with appropriate plus or minus indication of the divergence of true mortality above or below the expected mortality.

The expected mortality rate is calculated as follows:

The over-all mortality rate for each weight group as a base line is multiplied by the number of infants under consideration from that weight group. The sum of these figures is then divided by the total number of infants being considered from all weight groups to give the expected mortality rate. The actual calculation of expected mortality for male infants in our present series is given as an example:

$$\begin{aligned} 94\% \times 26 &= 2{,}444 \\ 64\% \times 49 &= 3{,}136 \\ 19\% \times 60 &= 1{,}140 \\ 6\% \times 252 &= 1{,}512 \\ 387 & \quad 8{,}232 \end{aligned}$$

$$\frac{8{,}232}{387} = 21\% \text{ expected mortality}$$

Effect of Sex

It is commonly accepted that male births exceed females in the ratio of 106 to 100.[19] We have noted again an excess of females over males in all but one of the premature weight groups with, however, a lower mortality rate

TABLE I. EFFECT OF SEX ON MORTALITY

	UNDER 1,000 GRAMS		1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS		TOTAL		MORTALITY PERCENTAGE		
	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	TRUE	EXP.	DEV.
Males.—													
1929-1938	0	16	4	14	25	17	122	13	151	63	30	25	+5
1941-1950	1	25	14	35	47	13	231	21	293	94	24	21	+3
Females.—													
1929-1938	1	16	9	11	38	11	140	10	189	50	21	25	−4
1941-1950	2	27	18	22	64	14	279	12	363	75	17	19.5	−2.5

among the females as is shown in Table I. Similar findings have been noted by others without specific explanation.[3, 4, 5, 10]

Length of Labor

Analysis of the length of labor, Table II, again shows little significant variation between true and expected mortality in the various time groupings. The "no labor" category, all abdominal deliveries, did show an increase of true mortality (27 per cent) over expected mortality (19 per cent) which was more marked than that noted previously (28 per cent true, 25 per cent expected). This again seems a consequence of the serious maternal indications for premature cesarean delivery such as abruptio placentae, placenta previa, toxemia, and diabetes, with the higher fetal risk attendant upon these conditions. Obviously, no conclusions may be drawn from the small group of cases in which length of labor has not been stated.

Type of Delivery

The type of delivery causes no great variation between true and expected mortality except in the cesarean section group, and in the version and extraction group. The latter is an even smaller group than in the previous study and cannot be considered statistically significant. The divergence between true and expected mortality for abdominal delivery has already received comment. It will be noted in Table III that breech delivery occurred in 11.7 per cent of our premature infants over the twenty years, whereas breech delivery represents only 3.5 per cent of all deliveries including deliveries of mature infants. Cesarean delivery was employed for 10.6 per cent of our twenty-year prematures, whereas its incidence is only 4 per cent for all infants. Forceps delivery was employed for 31 per cent of prematures as against 53 per cent of all infants delivered. Spontaneous delivery occurred more often among prematures than among all infants. The low true and expected mortality figures for forceps delivery reflect the greater employment of forceps delivery among the larger and therefore better-risk prematures. The forceps delivery of prematures has increased in the second ten years as the incidence of spontaneous delivery has decreased. In the 2,001 to 2,500 gram group, spontaneous delivery has had a slightly lower mortality rate than has forceps delivery, while forceps delivery gives a better figure for the 1,501 to 2,000 gram group. However, the differences are small and neither method would seem to offer any greater individual risk.

Breech delivery has been commonly considered to be more dangerous for prematures than have other forms of vaginal delivery.[2, 10, 18] The high expected mortality rate obtained and its close approximation to the true mortality rate would suggest that the peril in breech delivery is more a hazard of the smaller infants involved than of the presentation itself.[4]

Sedatives and Anesthesia

The effect of sedative or analgesic drugs and of anesthetic agents was next considered. It has been our general policy to employ analgesic drugs sparingly in premature labor except for the obviously larger infants. Although separate dosage listings were not made, in many if not most of these premature labors smaller doses of the analgesic drugs were used than are routinely given in term labor. Such drugs were employed in 24 per cent of the deliveries of infants under 1,000 grams, 33 per cent of the 1,001 to 1,500 gram group, 30 per cent of the 1,501 to 2,000 gram group, and 44 per cent of the 2,001 to 2,500 gram group. There was no great divergence between true and expected mortality figures in any of the statistically significant groups as shown in Table IV.

TABLE II. LENGTH OF LABOR

	1941-1950													1929-1938		
	UNDER 1,000 GRAMS		1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS		TOTAL		MORTALITY PERCENTAGE			MORTALITY PERCENTAGE		
	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	TRUE	EXP.	DEV.	TRUE	EXP.	DEV.
Under 5 hours	2	16	14	15	40	14	213	9	269	54	17	18	−1	28	25	+3
6-10 hours	1	14	7	17	32	6	145	8	185	45	20	20	0	23	21	+2
11-15 hours	0	6	6	6	8	3	51	2	65	17	21	23	−2	17	19	−2
16-20 hours	0	3	1	3	9	0	29	2	39	8	17	19	−2	26	23	+3
21 plus hours	0	4	1	6	10	0	24	1	35	11	24	25	−1	19	25	−6
No labor	0	4	3	3	9	3	36	8	48	18	27	19	+8	28	25	+3
Not stated	0	5	0	7	3	1	12	3	15	16						

TABLE III. TYPE OF DELIVERY

	1941-1950													1929-1938			PERCENTAGE DELIVERED BY METHOD			
	UNDER 1,000 GRAMS		1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS		TOTAL		MORTALITY PERCENTAGE			MORTALITY PERCENTAGE			PREMATURE 1929-1938	PREMATURE 1941-1950	PREMATURE 20 YEARS	ALL BABIES 1928-1948
	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	TRUE	EXP.	DEV.	TRUE	EXP.	DEV.				
Version and extraction	0	1	0	1	2	1	3	2	5	5	50	24	+26	38	33	+5	2.8	1.2	1.8	0.9
Breech	1	12	6	9	17	6	50	4	74	31	29	28	+1	27	24	+3	9.9	12.7	11.7	3.5
Cesarean	0	5	3	4	10	3	44	9	57	21	27	19	+8	28	26	+2	12.8	9.5	10.6	4
Forceps	0	4	1	10	42	8	223	10	266	32	11	11	0	11	14	−3	21.4	36	31	53
Spontaneous	2	30	22	32	40	9	190	8	254	79	23	25	−2	30	27	+3	51.5	40	44.4	38
Not stated	0	0	0	1	0	0	0	0	0	1										

TABLE IV. EFFECT OF SEDATIVE AND ANESTHESIA

	1941-1950												
	UNDER 1,000 GRAMS		1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS		TOTAL		MORTALITY PERCENTAGE		
	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	TRUE	EXP.	DEV.
None	0	7	2	4	2	1	3	2	7	14	66.6	54	+12.6
Conduction anesthesia	0	9	5	11	34	6	111	6	150	32	17.7	18.4	−0.7
Sedative only	0	3	3	2	1	0	5	1	9	6	40	44	−4
Inhalation anesthesia only	3	24	16	26	50	14	164	14	233	78	25	24.4	+0.6
Inhalation plus sedative	0	9	6	14	24	6	227	10	257	39	13	13.9	−0.9

Conduction Anesthesia.—
Local infiltration 5%
Spinal only 60%
Spinal and sedative 35%

Inhalation Anesthesia.—
Nitrous oxide analgesia
Ethylene
Cyclopropane

It will be noted that general anesthesia plus sedation was used primarily for delivery of the larger weight group, whereas conduction anesthesia and inhalation anesthesia alone were offered in greater proportion in all weight groups, as evidenced by the higher expected mortality figures obtained for these methods.

Since it has been our clinical impression that premature infants delivered under conduction anesthesia, primarily spinal anesthesia at our hospital, breathed and cried more promptly and exhibited better immediate vigor, we attempted to determine if the wider use of this anesthesia in the last three years of the study had brought about any significant decrease in actual mortality during this time. The infants were grouped in two-year chronologic periods again by weight groups, and the incidence of employment of conduction anesthesia in each period and weight group was determined. In Table V it is evident that the greatly increased use of conduction anesthesia in 1949 and 1950 did not lower the mortality rate significantly for any weight group and may even have increased it slightly. However, it is felt that a longer period of trial is essential to obtain a more significant series before venturing such a conclusion. It remains our impression that the premature infant delivered under spinal anesthesia responds more favorably at birth.

TABLE V. MORTALITY RATE AND CONDUCTION ANESTHESIA

	1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS	
	% MORTALITY	% CONDUCTION	% MORTALITY	% CONDUCTION	% MORTALITY	% CONDUCTION
1941-1942	64.3	0	23	0	7.5	1.5
1943-1944	60	10	3.5	0	6	1
1945-1946	62	5	25	0	1.5	0
Total	62	4.5	16	0	5	0.9
1947-1948	58	19	18	32	9	23
1949-1950	78	50	28	81	4	65
Total	66	39	22	52	7	60

In general, it has been our practice to begin the spinal anesthesia in both premature or term labors either in the second stage of labor or only at the very end portion of the first stage. Many writers have suggested that much of the benefit of conduction anesthesia for premature labors may derive from relatively early first stage institution of the anesthetic. A more orderly pro-

TABLE VI. EFFECT OF MATERNAL MORBIDITY

	1941-1950										MORTALITY PERCENTAGE						MORBIDITY INCIDENCE	
	UNDER 1,000 GRAMS		1,000-1,500 GRAMS		1,501-2,000 GRAMS		2,001-2,500 GRAMS		TOTAL		1941-1950			1929-1938				
	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	LIVED	DIED	TRUE	EXP.	DEV.	TRUE	EXP.	DEV.	'29-'38	'41-'50
No morbidity	3	27	15	28	65	16	374	15	457	86	16	17	−1	19.8	20.3	−0.5	63%	66%
Premature rupture	0	11	10	13	22	3	64	4	96	31	25	26.6	−1.6	31	27.5	+4.5	12.8%	15.4%
Toxemia	0	2	4	3	16	1	32	4	52	10	16	19	−3	22	26	−4	14%	7.5%
Abruptio placentae	0	1	0	3	0	1	7	4	7	9	56	23	+33	33	23	+10	1.3%	1.9%
Placenta previa	0	5	1	5	7	3	18	5	26	18	41	27	+14	60	49	+11	3.3%	5.3%
Hydramnios	0	3	0	1	0	1	0	0	0	5	100	27	+73	77	66	+11	2%	0.6%
Others	0	3	2	4	1	2	15	1	18	10	36	29	+7	36	36	0	4.2%	3.4%

gression of the first stage with diminished soft tissue resistance is claimed as the principal advantage of this method.[11] It may be the case that with earlier employment of the spinal anesthetic our mortality rates will decline.

Maternal Morbidity

Maternal morbidity was noted in 34 per cent of our present series, the figure for the first series being 37 per cent. Again, premature rupture of the membranes and toxemia showed a true fetal mortality slightly less than the expected figure. Mortality figures for abruptio placentae, placenta previa, and hydramnios all grossly exceeded the expected mortality. Table VI also reveals a marked reduction in the incidence of toxemia in the second series, from 14 per cent to 7.5 per cent.

Cause of Death

The autopsy rate among premature neonatal deaths has continued at 94 per cent. Since atelectasis, asphyxia, and congenital weakness are not considered primary anatomic causes of death, they have been classified in this study under the heading of prematurity. This group has accounted for only 54 per cent of the deaths in this series compared with 80 per cent of deaths in the previous study, if a similar classification is employed. No present attempt has been made to review these specimens to determine the incidence of a hyaline-like alveolar membrane. Arey and Dent[15] reported this finding in 75 per cent of premature infants considered to have died of asphyxia.

A definite anatomic cause of death was discovered in only 20 per cent of the cases in the first study. In this present series an anatomic cause was found in 46 per cent, reflecting greater accuracy of autopsy examination. The incidence of anatomic causes was as follows: birth injury 25.7 per cent, congenital anomaly 11.9 per cent, infection 5.7 per cent, and erythroblastosis fetalis 2.5 per cent.

Age at Death

A gratifying decrease in premature neonatal mortality from 25 per cent to 20 per cent has been noted. Study of the age at death in the second series shows a lessening of the death rate in the first twelve hours, and an increase of the death rates for all other categories until past ten days, where there is also a decided drop (Table VII). Better obstetrical management and improved immediate pediatric care have thus extended the life span of many babies formerly lost in the first twelve hours, some of whom must have survived their prematurity. Others, unfortunately, now succumb only a few hours later.

TABLE VII. ANATOMICAL CAUSES OF DEATH

AGE AT DEATH, 1941-1950. AUTOPSY RATE 94%							
	UNDER 12 HOURS	12-24 HOURS	24-48 HOURS	3-10 DAYS	OVER 10 DAYS	TOTAL	PERCENTAGE AUTOPSIES
Prematurity	54	23	6	2	1	86	54%
Birth injury	20	9	7	5	0	41	25.7%
Congenital anomaly	12	1	4	1	1	19	11.9%
Infection	3	1	1	4	0	9	5.7%
Erythroblastosis	2	1	0	1	0	4	2.5%
No autopsy	4	1	1	3	1	10	
Percentage, 1941-1950	56.2%	21.3%	11.2%	10%	0.1%		
Percentage, 1929-1938	72%	11%	6%	5%	5%		

Conclusions

1. Although the incidence of live births of premature infants has remained unchanged during the past ten years, the premature neonatal mortality is only 80 per cent of that in our previous experience.

2. Neonatal mortality among prematures continues to account for at least half of our total neonatal mortality.

3. Neonatal mortality in premature infants continues to vary inversely as the birth weight.

4. Premature births of female infants have again exceeded births of males, contrary to the usual ratio for all infants at birth.

5. Male premature infants have a higher mortality than the females.

6. Length of labor has had little apparent effect on infant mortality.

7. Cesarean section has continued to carry a disproportionately high mortality rate among prematures. The unusual maternal conditions often requiring premature abdominal delivery undoubtedly affect this rate adversely.

8. The type of vaginal delivery again has seemed to have no pronounced effect on mortality.

9. Breech delivery has occurred almost three times as frequently in prematures as in all infants.

10. The use of analgesic drugs has not shown an adverse effect on mortality, but their use in premature labors has been restricted as compared to that in term labors.

11. The employment of anesthetics for delivery did not increase mortality in this series. No special advantages of conduction anesthesia in terms of premature infant mortality have been demonstrable.

12. Morbidity was found in 34 per cent of mothers, but only placenta previa, abruptio placentae, and hydramnios seemed to cause an increased fetal mortality. Premature rupture of the membranes and toxemia caused no increased fetal risk per se.

13. The frequency of toxemia was only half that noted in a previous ten-year series.

14. An anatomic cause of death was demonstrable in 46 per cent of the infants who died as compared with 20 per cent in the previous group. Birth injury remained the largest single cause of death, after prematurity itself.

15. A definite shift in the time of death of premature infants has been noted, although 56 per cent of the deaths still occur in the first twelve hours.

16. No single obstetrical factor has been demonstrated as the cause for our decreased premature neonatal mortality. It seems likely that many obstetrical improvements, more skillful nursing care, and efficient pediatric supervision in the neonatal period have collectively accomplished this improvement.

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GYNECOLOGICAL LESIONS AND URETEROHYDRONEPHROSIS*

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THE association of gynecological lesions with dilatation of the upper urinary tract has been reported by many authors. As early as 1824, Froriep[1] reported damage to the urinary tract due to prolapse of the uterus. In 1846 Virchow[2] described prolapse with ureteral dilatation. Halban and Tandler[3] (1907) reported dilatation of the ureter in 15 of the 23 cases of prolapse which they studied. They believed that the dilatation was due to compression and angulation of the ureter against the margin of the levator sling when prolapse occurred. Mirabeau,[4] in 1908, described dilatation of the kidney pelves in 3 cases of prolapse and 3 cases of cystocele. Hirokawa,[5] Sellheim,[6] Young,[7] and Frank[8] have all reported dilatation of the urinary tract in autopsy material that they have analyzed. In 1923 Brettauer and Rubin[9] carried out a clinical study on a group of 10 patients with uterine prolapse and found ureterohydronephrosis in 8 of their 10 cases. They stressed the importance of the study of renal function and search for infection in these patients. The frequent finding of ureterohydronephrosis in pregnancy has been emphasized by many authors,[10, 11] but this problem does not concern us in the present study.

Material

The purpose of this study has been to analyze 218 cases among 5,600 patients admitted to the Gynecological Service of the Mount Sinai Hospital between 1940 and 1948. These patients, not representing a consecutive series, presented a variety of lesions of the pelvic viscera or pelvic supports. They were chosen because they had had a study of the urinary tract, in most instances, by intravenous pyelography. In some cases cystoscopy and retrograde pyelograms have been performed. Clinical impressions have been confirmed by operative findings and correlated with pathological reports. These cases have been studied under the following categories:

I. Prolapse of the uterus
II. Cystocele without prolapse
III. Fibromyomas of the uterus
IV. Neoplasms of the ovary and parovarium
V. Malignancy of the uterus
VI. Pelvic inflammatory disease
VII. Cases of urinary tract infection or impairment of renal function
VIII. Regression of ureterohydronephrosis following correction of the gynecological lesion

Prolapse of the Uterus

In this series, 68 cases of uterine prolapse have been classified under their appropriate headings ranging from first-degree prolapse with the cervix descending to the introitus through third-degree prolapse including complete procidentia with eversion of the vagina. The following factors have been analyzed: (1) the degree of prolapse, (2) the duration of prolapse, (3) the presence or absence of cystocele, (4) the incidence of urinary tract infection, (5) the incidence of impairment of renal function, (6) the occurrence of hyper-

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tension, (7) the parity of the patients with prolapse, and (8) the follow-up results in these patients.

Throughout this study the degree of ureterohydronephrosis has been tabulated as: "none," "slight," "moderate," "marked," exactly as reported by the department of roentgenology. Table I shows the prolapse cases and the incidence and degree of urinary tract dilatation.

TABLE I. PROLAPSE OF THE UTERUS

DEGREE OF PROLAPSE	NUMBER OF CASES	URETEROHYDRONEPHROSIS				INCIDENCE	
		NONE	SLIGHT	MODERATE	MARKED		
First degree	20	19	1	0	0	1:20	5%
Second degree	23	17	3	3	0	6:23	26%
Third degree	25	15	7	1	2	10:25	40%
All cases	68					17:68	25%

1. Degree of Prolapse.—Although the series is not large, it appears that the more marked the prolapse the higher the incidence and the greater the severity of the ureterohydronephrosis.

2. Duration of Prolapse.—In a study of the length of time that the prolapse was complained of, the shortest duration was found to be one month and the longest 30 years. The average duration of prolapse in this group was 6.5 years. From the data analyzed it did not seem that the duration of prolapse directly influenced the incidence or degree of ureterohydronephrosis. Thus, the two cases with marked dilatation of the upper urinary tract had noticed prolapse of only two and three years' duration, whereas two patients with prolapse for twenty and thirty years showed no ureterohydronephrosis.

3. The Presence or Absence of Cystocele.—Sixty-five of the 68 prolapse cases were associated with cystocele ranging from small to huge. In the 3 remaining cases no cystocele was present. Cystocele was apparently not a significant factor in the frequency of occurrence or degree of ureterohydronephrosis. The same conclusion may be drawn from a separate study of a group of 13 patients having cystocele without prolapse. Only one among these showed a slight degree of dilatation.

4. The Incidence of Urinary Tract Infection.—Four patients, all of whom had third-degree prolapse of many years' standing, had infection of the upper urinary tract. This subject will be considered in greater detail under a separate heading.

5. The Incidence of Impairment of Renal Function.—Only 1 patient in this prolapse series (Case 161, L. K., admission No. 543750) showed definite evidence of impaired renal function. This patient, whose case was reported in detail by Frank,[27] had an irreducible prolapse in addition to a large granulosa-theca-cell tumor of the ovary. She improved after removal of the tumor, and, subsequently, repair of the prolapse. Several reports of fatal uremia due to prolapse have been published by Frank,[8] Young,[12] Altschul,[13] and Wallingford.[14] Our experience with these recent cases, studied in the past eight years, would lead to the conclusion that our patients have sought medical attention earlier than in former years.

6. The Occurrence of Hypertension.—It has been postulated by Wosika and Maher[15] that patients with prolapse develop hydronephrosis and then hypertension. An analysis in our series of 197 patients with and without prolapse showed no significant difference in the average blood pressure readings, regardless of the status of the upper urinary tract.

7. Parity of Patients With Prolapse.—Analysis showed the average parity of the 48 patients with no hydronephrosis to be 2.7, while in the 20 patients with hydronephrosis the average parity was 4.0.

8. Follow-up Results.—In these 68 patients the treatment was as follows: (a) 58 parametrial fixation operations (including 2 operations on prolapsed cervical stumps following subtotal hysterectomy and one operation for recurrent prolapse); (b) 6 patients were fitted with pessaries because of medical contraindications to operation; (c) 1 patient had a Le Fort operation; (d) 1 patient had a vaginal hysterectomy and posterior colporrhaphy; (e) 2 patients had large pelvic tumors and improved after laparotomy and removal of the pelvic lesions.

Fig. 1.—Mild ureterohydronephrosis associated with third-degree prolapse. Descent of ureters and vesical calculus visualized.

Follow-up studies on these patients revealed good results from the anatomical and functional points of view. In our series, 40 per cent of the patients with third-degree prolapse developed upper urinary tract dilatation. Operative correction, performed when necessary under local anesthesia, gave excellent results. Where contraindication to operation existed, a supporting pessary was fitted. Undue delay in correcting the prolapse may result in permanent renal damage. Danforth[29] has stressed this point. Fig. 1 shows a mild degree of dilatation of the urinary tract associated with third-degree prolapse. In this patient a large vesical calculus was also present. The marked descent of the ureter is well demonstrated in the intravenous urogram. This "downward kinking" of the lower ureters has been emphasized by Lieberthal and Frankenthal[28] in their studies on the mechanism of ureteral obstruction in prolapse of the uterus.

Cystocele Without Prolapse

Thirteen cases of cystocele, ranging from "slight" to "huge," and in duration from 2 months to 17 years, have been studied. One patient was described as showing a slight degree of ureterohydronephrosis on intravenous urography. A second had a large cervical myoma and moderate cystocele. In this patient the dilatation of moderate degree was considered due to the myoma, rather than to the cystocele, and total hysterectomy was performed. The remaining 11 cases of cystocele showed no ureterohydronephrosis.

Fibromyomas of the Uterus

In Table II, 56 patients with fibromyomas of the uterus have been studied. Twenty-five of these patients manifested some degree of dilatation of the upper urinary tract as revealed by intravenous pyelography. From these data it will be noted that the incidence of ureterohydronephrosis is markedly increased when fibroids are larger than the size of a six months' gestation, or developed in the cervix, or associated with adnexal disease. This is in accord with the conclusions of Everett and Sturgis,[17] Kretschmer and Kanter,[19] and Morris and Juracsek.[30]

TABLE II. FIBROMYOMAS OF UTERUS

FIBROIDS	NUMBER OF CASES	URETEROHYDRONEPHROSIS				INCIDENCE	
		NONE	SLIGHT	MODERATE	MARKED		
Fibroids (size less than 6 months' gestation)	32	21	7	3	1	11:23	34%
Fibroids (size larger than 6 months' gestation)	12	5	7	2	2	7:12	58%
Fibroids (cervical)	5	2	2	0	1	3:5	60%
Fibroids (with adnexitis)	7	3	1	2	1	4:7	57%
All cases	56					25:56	45%

Other Gynecological Lesions

In Table III, 71 patients with benign, malignant, or inflammatory lesions of the pelvic organs are tabulated. In studying the benign ovarian tumors it was found that the larger cysts and those located deep in the pelvis had a greater tendency to produce ureterohydronephrosis of marked degree. Prompt regression of urinary tract dilatation was observed following removal of these cysts. This subject will be considered under a separate heading.

TABLE III. GYNECOLOGICAL LESIONS AND URETEROHYDRONEPHROSIS

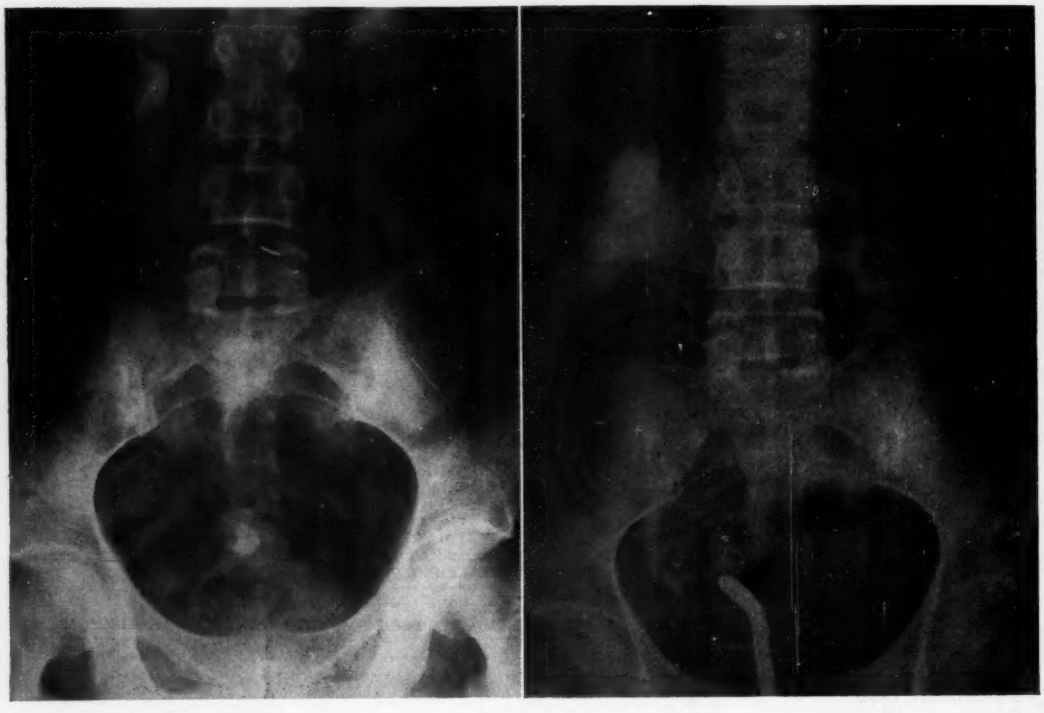
LESION	NUMBER OF CASES	URETEROHYDRONEPHROSIS				INCIDENCE	
		NONE	SLIGHT	MODERATE	MARKED		
Benign ovarian neoplasms	25	17	3	3	2	8:25	32%
Parovarian cysts	2	1	0	1	0	1:2	50%
Carcinoma of ovary	12	5	1	4	2	7:12	58%
Carcinoma of cervix	12	7	1	1	3	5:12	42%
Carcinoma of fundus	5	3	1	1	0	2:5	40%
Pelvic inflammatory disease	15	9	1	2	3	6:15	40%

Of the 12 ovarian carcinoma cases, 7 showed some urinary tract dilatation. This figure is in close agreement with the findings of Long and Montgomery,[20] who reported ureteral obstruction in 9 of 13 cases.

Only 12 patients with cervical cancer have been studied in this series. Of these 1 showed slight, 1 showed moderate, and 3 showed marked ureterohydronephrosis. The patients with marked dilatation all had Stage III or Stage IV neoplasms with extensive parametrial involvement. Ureteral obstruction has been described in from 50 per cent to 80 per cent of patients with carcinoma of the cervix. Graves, Kickham, and Nathanson[21] in 1936 reviewed 257 such cases and found that "more than 70 per cent had obstruction of the ureters." Our low incidence is probably explained by the small size of our series, and, possibly, we have seen earlier cases in the past eight years than those reviewed fifteen and twenty years ago.

The frequency of ureteral obstruction producing terminal uremia in carcinoma of the cervix is too well known to require emphasis. The development of ureterohydronephrosis resulting from cervical carcinoma is illustrated by comparing Fig. 2, *A*, the pyelogram done in September, 1946, with Fig. 2, *B* taken in February, 1947. Urinary tract complications in relation to carcinoma of the cervix are so significant that before radiotherapy or surgery is undertaken a study of the bladder, ureters, and kidneys should be done.

In our carcinoma group we are dealing with only a few cases, but it is interesting to note that the incidence is close to that in the conclusions of others.[20] Our 2 patients with urinary tract dilatation both had extension of the disease into the cul-de-sac and broad ligament.



A. *B.*

Fig. 2.—*A*, Normal intravenous pyelogram, September, 1946. Carcinoma of cervix. *B*, Right ureterohydronephrosis, February, 1947. Carcinoma of cervix. (Same patient as in Fig. 2, *A*.)

Of the 15 patients with pelvic inflammatory disease, 6 showed some dilatation, an incidence of 40 per cent. Two of the patients included in this group also had pelvic endometriosis—one showed slight, and the other moderate dilatation. The incidence found here agrees with the reports in the literature, and the finding of hydronephrosis associated with pelvic endometriosis is in keeping with the paper published by Leventhal and Solomon.[22] Randall,[23] O'Conor and Greenhill,[24] and Goodall[25] have all described endometriosis involving the ureter with fatal uremia in several cases.

In 1937, I[26] reported a case of marked ureterohydronephrosis resulting from extensive pelvic inflammatory disease. There was definite evidence of impairment of renal function. Under conservative therapy, there was improvement in the inflammatory process and, simultaneously, definite regression of the urinary tract dilatation and distinct improvement in renal function.

The frequency and extent of hydronephrosis in relation to pelvic inflammatory disease should make the internist, as well as the gynecologist, alert to the possibility of renal dilatation or damage. With chemotherapy and antibiotics, appropriate treatment, both medical and surgical, can save these patients with benign lesions from incapacitating illness. Fig. 3 shows an intravenous pyelogram demonstrating ureterohydronephrosis resulting from pelvic inflammatory disease.

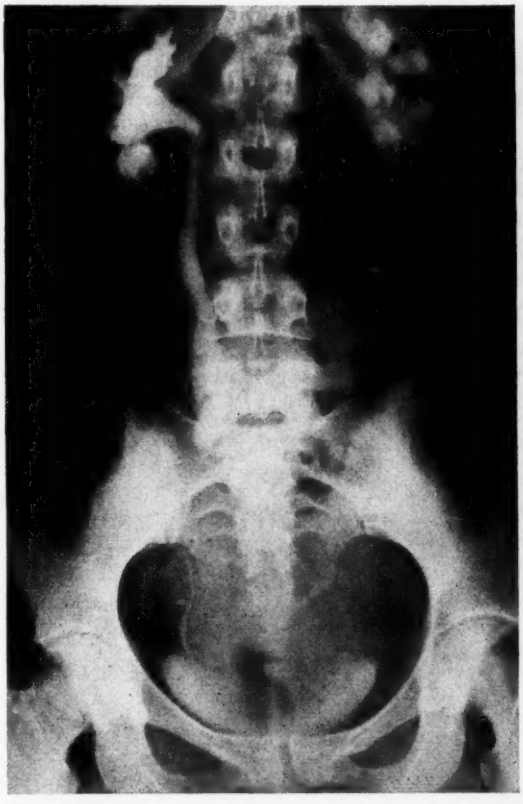


Fig. 3.—Ureterohydronephrosis associated with pelvic inflammatory disease.

An interesting observation in regard to pelvic inflammatory disease indicates that, whereas urinary tract dilatation disappears promptly after the removal of ovarian cysts and fibroids in approximately 75 per cent of the cases, only about 40 per cent of the cases of inflammatory disease revert to normal within a few months. This slow regression, if it occurs at all, in the inflammatory group, has been emphasized by Everett and Scott[16] and Everett and Sturgis.[17] The conclusion of most writers on the subject is that removal or spontaneous regression of pelvic inflammatory masses does not cure scarring, or dense adhesions around the ureter, and dilatation therefore persists for some time or remains indefinitely. This, too, is a strong argument in favor of early recognition and prompt treatment of pelvic inflammatory disease before renal damage has occurred.

Infection and Impairment of Renal Function

In Table IV the data concerning the 12 patients in this series manifesting urinary tract infection or impairment of renal function have been tabulated in

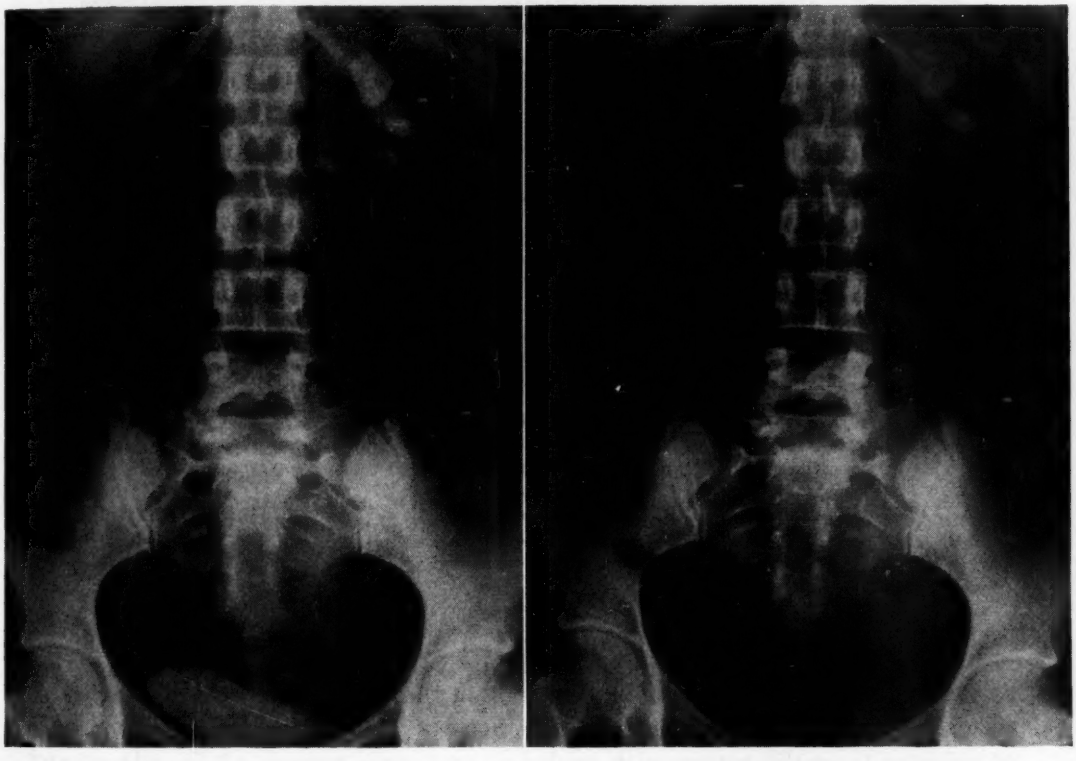
some detail. A review of these cases, particularly the benign lesions, producing infection or impaired renal function, emphasizes the importance of the early recognition of urinary tract complications and the need for prompt treatment of the underlying gynecological condition.

TABLE IV. GYNECOLOGICAL LESIONS CAUSING URINARY TRACT INFECTION AND/OR IMPAIRMENT OF RENAL FUNCTION

CASE NUMBER	GYNECOLOGICAL LESION	INFECTION OF GENITOURINARY TRACT	IMPAIRED RENAL FUNCTION	COURSE
6 A. S. (562144)	Carcinoma of cervix, Stage III	None	Nonfunctioning right kidney; dilated left kidney	Uremia, fatal, 4 months
38 E. T. (473307)	Huge, degenerating myosarcoma of uterus	Marked	Poor renal function. No visualization on intravenous pyelogram. Blood urea 49 mg.	Terminal uremia
47 M. P. (478750)	Third degree prolapse, 15 years	Marked, with 40 vesical calculi	Marked ureterohydronephrosis	Died, postoperative peritonitis after vaginal cystotomy
119 F. A. (530751)	Third degree prolapse, 10 years	Moderate	Slight dilatation, bilateral	Parametrial fixation operation. Cured
120 S. T. (530566)	Fibroid uterus, size of 4 months' gestation	Mild	Moderate dilatation, bilateral	Hysterectomy. Cured
161 L. K. (543750)	(a) Large granulosa-theca-cell tumor of ovary. (b) Third degree prolapse (irreducible) 2 years	Marked	Marked bilateral ureterohydronephrosis	(a) Removal of tumor. (b) Parametrial fixation operation for prolapse. Improved.
170 T. V.	Metastatic adenocarcinoma infiltrating cul-de-sac	Mild	Dilated kidney pelves, bilateral	Exploratory laparotomy. Downhill course.
171 E. B. (563848)	Carcinoma of ovaries	Moderate	Dilatation right kidney pelvis, moderate	Hysterectomy, bilateral salpingo-oophorectomy. Radiotherapy. Improved. No evidence of disease 20 months after operation.
177 B. S. (569907)	Carcinoma of ovaries	Marked	Anuria, azotemia. Blood urea 112 mg.	Hysterectomy, bilateral salpingo-oophorectomy. Massive postoperative embolism. Autopsy, marked bilateral ureterohydronephrosis
178 L. R. (571100)	Pelvic inflammatory disease, fibroids, endometriosis, left tubovarian abscess	Marked	Marked left ureterohydronephrosis	Hysterectomy, left salpingo-oophorectomy, right salpingectomy. Improved.
199 F. K. (477606)	Large pelvic exudate following hysterectomy	Mild	Moderate dilatation right upper urinary tract	Improved spontaneously
206 A. L. (576291)	Third degree prolapse, 15 years	Moderate with vesical calculus	Mild ureterohydronephrosis, bilateral	(1) Litholapaxy. (2) Le Fort operation. Improved

Regression of Dilatation Following Therapy

Most of the patients we have had the opportunity of restudying following appropriate gynecological therapy have shown regression of the ureterohydronephrosis. This has been particularly true following the removal of fibroids and ovarian cysts and after correction of uterine prolapse. Our series is small but follow-up figures approximate 75 per cent improved. This is very close to the data quoted by Kretschmer and Kanter,[19] and Everett.[11] Subsidence of urinary tract dilatation resulting from pelvic inflammatory disease occurs in a smaller percentage of the cases, approximately 40 per cent, after treatment (surgical or conservative), and the process of regression is a slower one. Figs. 4 and 5 are pre- and postoperative pyelograms demonstrating the diminution of ureterohydronephrosis after surgery.



A. *B.*

Fig. 4.—*A*, Left ureterohydronephrosis with tubovarian abscess (Oct. 10, 1947). *B*, Disappearance of left ureterohydronephrosis associated with left tubovarian abscess. Intravenous pyelogram, Oct. 10, 1947, seventeen days after operation.

This study would not be complete if the incidence of hydronephrosis and ureterohydronephrosis among the general population were not considered. The standard texts (Everett,[11] Keyes,[31] Lowsley and Kirwin,[32] and Hinman[33]) have all discussed this point. The largest series of cases mentioned is that of Morris (quoted by Hinman) who found 381 cases of hydronephrosis in 6,536 patients examined, an incidence of 5.8 per cent. In our series, 73 of 218, or 33.5 per cent of the cases studied, showed hydronephrosis. Contrary to our cases of acquired dilatation, congenital hydronephrosis is nearly always associated with (a) aberrant vessels, (b) stricture, kink, or other anomalies of the ureter, or (c) nephroptosis. These conditions, as well as intrinsic disease

of the urinary tract, were ruled out by the x-ray and urologic departments of the hospital, without whose cooperation this study could not have been undertaken.

A. *B.*

Fig. 5.—*A*, Right ureterohydronephrosis (and double ureter) associated with fibroids. Intravenous pyelogram, Oct. 27, 1947.

B, Disappearance of ureterohydronephrosis three weeks after removal of fibroids. Intravenous pyelogram, Nov. 12, 1947.

Summary

A group of 218 gynecological patients presenting various lesions of the pelvic organs has been studied to determine the relationship between gynecological conditions and ureterohydronephrosis. The frequency of occurrence of urinary tract dilatation with prolapse, cystocele, tumors of the uterus and ovaries, and pelvic inflammatory disease has been noted. The importance of prompt treatment of the conditions has been emphasized.

Conclusions

1. Prolapse of the uterus produced ureterohydronephrosis in 25 per cent of our cases. The incidence and severity of urinary tract dilatation increased with the degree of prolapse. Early correction of prolapse by surgery or by pessary is indicated to avoid ureterohydronephrosis, infection, and renal damage.

2. Cystocele without prolapse did not appear to be a significant factor in the production of ureterohydronephrosis.

3. Fibromyomas of the uterus produced ureterohydronephrosis in 45 per cent of our cases. Large fibroids, cervical fibroids, and those associated with

adnexitis caused urinary dilatation almost twice as frequently as smaller fibroids.

4. Benign neoplasms of the ovary produced ureterohydronephrosis in 32 per cent of the cases while malignant lesions caused dilatation in over 58 per cent.

5. Carcinoma of the cervix with parametrial involvement may cause hydronephrosis in 70 per cent of cases, whereas carcinoma of the fundus causes urinary tract dilatation less frequently, in 40 per cent.

6. Pelvic inflammatory diseases and endometriosis caused urinary tract dilatation in more than 40 per cent of the patients studied.

7. Twelve cases manifesting urinary tract infection or impairment of renal function have been summarized.

8. Regression of ureterohydronephrosis following correction of benign gynecological lesions occurs promptly in 75 per cent of patients. In cases of pelvic inflammatory disease regression is slower and occurs in only 40 per cent of cases.

The author wishes to express his thanks to Dr. M. A. Goldberger, Attending Gynecologist, Mount Sinai Hospital, New York City, for his valuable assistance, and to Dr. Jack Burke of the Resident Staff, for his help with the charts.

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PELVIC TUBERCULOSIS

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THE management of pelvic tuberculosis has been a controversial subject for several years. There is a wide diversity of opinion as to incidence, diagnosis, classification, and treatment.

Incidence

Halbrecht[1] of Tel Aviv reported upon a study of 820 women who had been sterile from 2 to 8 years. Their ages ranged from 19 to 43 years. In each case, endometrial biopsies were done to determine whether ovulation had taken place. Tuberculous endometritis was reported in 5.5 per cent of the cases. It is reasonable to assume that had the curettage been complete rather than partial the incidence probably would have been much greater. These findings are significant because not a single clinical sign of genital tuberculosis was present prior to curettage. He concludes that genital tuberculosis is much more common in apparently healthy women than is generally supposed. This is especially true in sterile women. In a series of 54 patients with complete obstruction of the Fallopian tubes, Halbrecht found endometrial tuberculosis in 33⅓ per cent of the cases. Sharman[2] of Glasgow found tuberculosis in 5 per cent of 800 endometrial specimens removed for biopsy. In Australia, Grant and Mackay[3] found it in 1 per cent. Sharman believes that the disparity in these results is due to the fact that Grant and Mackay studied too little of the endometrium.

Novak[4] states that any portion of the female genitals may be invaded by the tubercle bacillus, but by far the most frequent and usually the initial seat of involvement is the Fallopian tube. In other words, tuberculosis of other parts of the genital tract is usually secondary to tubal tuberculosis. The modes of infection are as follows:

1. Hematogenous, secondary to a focus in some other organ, usually the lung, which may have active or inactive disease.
2. By direct extension from abdominal tuberculosis.
   - A. By continuity.
   - B. By perforation of tuberculous intestinal ulcers or mesenteric lymph nodes (rare).
3. Primary (smallest group) infection of the genital tract from without. This etiology is difficult to prove (husband with genitourinary tuberculosis or pulmonary tuberculosis).

Norris[5] states that tuberculous salpingitis comprises 5 to 7 per cent of all cases of salpingitis. The Fallopian tubes are invaded in 85 to 95 per cent of genital tuberculosis; the endometrium in 35 to 50 per cent; and the ovaries in 6 per cent.

This paper is based on an analysis of 44 cases. Forty-three are from the Gynecological Service of the Harlem Hospital. These include the 22 cases

presented by Murray,[6] seen during the period 1931 to 1941. Twenty-one cases were seen during the period from 1942 to 1951. The other case was in a private patient of the senior author. During these 21 years, there were 29,377 admissions to the Gynecological Service. Forty-three of these were histologically verified genital tuberculosis, an incidence of 0.11 per cent.

Classification

A gross recognition of pelvic tuberculosis is important. In many cases, it is only after the abdomen is opened that a tuberculous infection is suspected or recognized. In our cases, we have seen the following gross pathological types:

1. Ascitic Type.—This type presents tubercles, fluid (ascites), a few friable adhesions, and little or no involvement of the genital organs. This is probably better called peritoneal tuberculosis.

2. Tubal Type.—This is limited principally to the tube. The gross appearance of tuberculous Fallopian tubes is strikingly similar to that caused by gonorrhea. Frequently, however, the fimbriae are not inverted, and the ostium remains patent, but is plugged with inspissated, caseous material. In many cases, the disease is limited to the tubal mucosa, and may result in a huge double pyosalpinx without much involvement of the peritoneum. In other instances, the infection traverses the wall of the salpinx, producing a thickened tube with tubercles throughout the musculature and interstitial tissues, and only slight dilatation of the lumen. It may also progress irregularly down the Fallopian tube producing nodules (salpingitis nodosa). In this type there are some tubercles on the serosal portion of the tube.

3. Advanced Type.—This type is subdivided into quiescent stage and progressive stage.

A. Quiescent or attempted healing stage: There is initial spread to all pelvic organs. Then there is attempted healing. Adhesions are usually of the type easily separated by blunt dissection. However, if there have been alternating phases of progression and healing, dense adhesions are found. They are very difficult to separate, but by sharp dissection a plane of cleavage may be found and the factors isolated.

B. Progressive stage: The tubercles spread, coalesce, and break down instead of entering a quiescent phase. Thus, the process becomes progressively destructive. The tuberculous areas undergo necrosis and caseation, dense adhesions form, collections of tuberculous pus appear, and all the pelvic structures become bound together into an irregular mass. With these tuberculous adhesions, lines of cleavage are lost owing to subperitoneal infiltration and destruction. Separation of intestinal adhesions is fraught with great danger because of the possibility of making an opening into the bowel, thereby establishing a permanent fecal fistula.

Table I shows the pathologic types in our series.

Most authorities state that the ovary is quite resistant to tuberculosis. However, we found the ovaries involved in 34 per cent of the cases. Whether this occurs by direct extension or through the lymphatics is not known.

TABLE I

TYPE	NUMBER OF CASES	PERCENTAGE
1. Ascitic	2	4.44
2. Tubal	22	48.89
3. Advanced		
A. Quiescent	11	24.44
B. Progressive	7	15.56
4. Uterine (microscope)*	3	6.67

*Uterine Type. This is a special group usually diagnosed by microscopic study of cervical or endometrial biopsy, or surgical specimen. The origin may be infection of the genital tract from sources external to the host. Cases in which the endometrium or cervix is involved by downward extension from tubal involvement are not included in this group. Only 3 cases of the uterine type were encountered in our series.

Table II shows the incidence of involvement of the various pelvic structures in our series, and the cases of Sered and Falls.[7]

TABLE II

	TUBE	ENDOMETRIUM	OVARY	CERVIX	MYOMETRIUM
Harlem Hospital 45 cases	88.89%	17.78%	40.00%	8.89%	15.56%
Sered and Falls[7] 16 cases	93.75%	75.00%	18.75%	12.5 %	Not given

In 571 autopsies performed on tuberculous females, Auerbach[8] found that 52 (9.1 per cent) had genital tuberculosis. The incidence of involvement of the pelvic organs was: tubes, 94.2 per cent; uterus, 55.7 per cent; ovaries, 26 per cent; vagina, 3.6 per cent.

Diagnosis

The diagnosis is difficult. Some cases of tuberculous salpingitis show no symptoms, the only clue being a history of sterility. Most cases that come to treatment because of symptoms are diagnosed as fibroid chronic inflammatory disease, or both. These cases are operated upon because of the feeling that surgery is indicated for large fibroids or disabling chronic adnexal diseases. Only when the pelvic structures are visualized can tuberculous salpingitis be suspected, and later proved by microscopic study of surgical specimens. Were it possible to diagnose pelvic tuberculosis prior to surgery, proper treatment could be effectively planned. With proper knowledge of the gross appearance of pelvic tuberculosis, better evaluation of the type of surgery to be done is possible.

In the typical case we find lower abdominal pain and tenderness of long duration, associated with one or more of the following complaints: fatigue and inability to work regularly, vaginal discharge, menstrual disturbances, weight loss, chills and fever, cough, night sweats. The patient is usually in the childbearing age and has no children.

Certain physical findings should alert the examiner to think of pelvic tuberculosis. Adnexal inflammatory masses in virgins must be regarded with suspicion. When present, the finding of a characteristic doughy abdomen is of great value. An indurated pelvis, which at times is insensitive and does not correspond to the temperature and sedimentation rate, points to a possible diagnosis of tuberculosis. Pelvic inflammation which does not improve under

sulfonamide and antibiotic therapy may be due to tuberculosis. Ascites is sometimes found.

An endometrial biopsy, when positive, is pathognomonic. Demonstration of the tubercle bacillus in the cervical discharge is rarely successful; culture of the menstrual discharge may show the tubercle bacillus. Tuberculin tests are of questionable value. We recommend routine chest x-ray for possible source and x-ray of the spine for possible spread, in all cases of suspected pelvic tuberculosis. Studies of genitourinary and gastrointestinal tracts should be made by smears, cultures, and guinea pig inoculations.

Treatment

We are interested principally in the advanced type. The patient has suffered from crippling pelvic infection over a long period of time. There is diffuse spread of the disease to all the pelvic viscera, with masses, induration, and thickening of the parametrium.

Formerly the final diagnosis in these cases was made at the autopsy table. The purpose of this paper is to make a plea for the salvage of some of these women who heretofore were doomed to suffering and disability until death. In these cases, surgery is the treatment of choice. We are in agreement with Sered and Falls[7] that the preferred surgical treatment is total hysterectomy and bilateral salpingo-oophorectomy. When total hysterectomy is not advisable because of technical difficulty, subtotal hysterectomy should be done. We strongly advise against abdominal drainage because of the tendency toward sinus formation. When drainage seems advisable due to uncontrollable oozing, packing and vaginal drainage may be resorted to with no adverse results.

We recognize the difficulty of the type of surgery recommended in these cases, and advise against its indiscriminate use by the occasional surgeon. We feel that this ablation surgery is justified on the following grounds:

1. These patients are chronically ill and unable to perform their duties in the home, or to work.

2. With the advanced type of pelvic tuberculosis, pregnancy is practically impossible.

3. The ovary is involved in a larger percentage of cases than was formerly believed, and should be removed.

4. If this focus of infection is left alone, it may spread to other parts of the body, especially the urinary and skeletal systems. Furthermore, even when it remains localized, the extensive inflammatory process with destruction of tissues exerts a constant drain on the body's physiologic functions and protective forces against disease.

5. The patients operated upon were showing no response to conservative therapy, and were growing progressively worse, making surgery the only chance for improvement.

Cases

The following case is an example of the advanced progressive type of pelvic tuberculosis:

B. J., Case No. 48-21187, a 23-year-old, single Negro nullipara, was admitted to the medical service on Jan. 29, 1948. She gave a history of night sweats and chronic cough of two months' duration, and a weight loss of 25 pounds during this period. Her last menstrual period was 3 months prior to admission. Medical work-up did not reveal any apparent cause for the patient's symptoms. A diagnosis of pregnancy was made, and the patient was transferred to the obstetrical service on Feb. 7, 1948. Abdominal examination revealed a cystic mass in the right lower quadrant. The pelvic findings were: a slightly enlarged retroverted uterus, the right fornix contained an indurated, cystic mass measuring about 10 cm. in diameter, tenderness and induration in the left fornix, and thickening and induration of the parametrium.

Laboratory findings were: secondary anemia; erythrocyte sedimentation rate 18 mm. in 24 minutes; normal urine. Chest x-ray showed normal lungs.

A diagnosis of right tubovarian abscess, possibly tuberculous, was made, and the patient was transferred to the gynecological service on March 1, 1948. She underwent surgery on March 17, 1948.

Operative findings were: Omentum and bowel matted together and adherent to the bladder and pelvic organs; numerous small, grayish-white nodules on all serosal surfaces; a right tubovarian abscess measuring 4 by 7 cm. and containing caseous material; a left pyosalpinx, and a normal-sized uterus. A total hysterectomy and bilateral salpingo-oophorectomy were done. The patient was placed on streptomycin, 1.0 Gm. daily, postoperatively. The postoperative course was uneventful except for febrile morbidity during the first 5 days. The temperature was septic in type, reaching at times to 104° F. She was discharged on the fourteenth postoperative day. The temperature was normal, the wound healed. She had no complaints.

The pathologic report was: Tuberculosis of tube, ovary, uterine wall, omentum, and peritoneum. There were areas of caseation in tube and omentum.

The patient was contacted 2½ years later; she was free of symptoms and satisfactorily employed as a machine operator.

The following case, in a private patient of the senior author, illustrates (1) the eventual need for surgery in some cases, (2) an unusual complication of pelvic tuberculosis, namely, rupture of tuberculous tubovarian abscess, and (3) spread of tuberculosis to the osseous system.

A. V., a 23-year-old white nullipara, was first seen in May, 1942, complaining of pain in the lower abdomen and irregular painful menses, varying from 2 to 3 months of amenorrhea to metromenorrhagia. Three months previously the patient had pleurisy. X-ray of chest and sputum studies at that time were negative for tuberculosis.

The general physical examination was negative. Pelvic examination revealed a virginal introitus, normal cervix, and corpus displaced to the left. There was a tender mass about 7 cm. in diameter in the right fornix and cul-de-sac. A diagnosis of pelvic tuberculosis was made, and conservative treatment was advised.

Seventeen months later, Oct. 6, 1943, the patient was hospitalized because of constant pain in the lower abdomen and menorrhagia. Pelvic examination revealed a small, retroverted uterus. On the posterior surface of the uterus there was an adherent mass which was interpreted to be an ovary. A diagnosis of acute appendicitis was made. At surgery, the abdomen was full of dense adhesions which were freed by sharp dissection. The uterus was small and retroverted. Both ovaries were normal in size. There was no evidence of active tuberculosis. The appendix was retrocecal and bound down, and showed signs of an inflammatory process. A Baldy-Webster suspension and appendectomy were performed. The pathologist reported chronic appendicitis. The postoperative course was uneventful, and the patient was discharged on the eleventh postoperative day.

On March 16, 1944, the patient was again admitted to the hospital with severe pain in the lower abdomen, chills, temperature ranging between 101 and 104° F., of two weeks' duration. The patient was acutely ill. The abdomen had a doughy feel, and was markedly tender throughout. A mass filled the right half of the abdomen. Pelvic examination

showed the uterus to be small and anterior. The right fornix and cul-de-sac were filled with an extremely tender mass extending 6 cm. above the umbilicus. The left fornix contained a tender, indurated mass.

Laboratory findings: Urine negative. Blood count: hemoglobin 82 per cent, red blood cells 4.11 million, white blood cells 19,800. Differential: lymphocytes 17 per cent, segmented polymorphonuclear leukocytes 83 per cent. Erythrocyte sedimentation rate 18 mm. in 15 minutes. X-rays of the chest and spine were negative.

The patient ran a septic temperature varying from 100 to 104° F. Several courses of sulfonamides had no favorable effect on her condition which became progressively worse. An evaluation of the condition of the patient after 2 weeks of conservative treatment led to the impression that she was suffering from a chronic tubovarian disease, probably tuberculous. On the fifteenth day of hospitalization, the temperature rose to 105° F. The patient complained of severe pain and went into shock. Abdominal examination did not reveal the same mass which had been outlined previously. A diagnosis of ruptured tubovarian abscess was made. A transfusion was started, and the patient was prepared for immediate laparotomy. At operation, there were extensive thick adhesions binding the small and large intestines, uterus, and adnexa into a large mass. Upon separation of some of the loops of intestine by sharp and blunt dissection, there was a gush of pus. After most of the adhesions were separated, a huge mass was found on top and to the right of the uterus. This had a perforation posteriorly (the usual site) through which purulent, caseous material exuded. The entire pelvis was indurated. All of the uterus, except the rim of the cervix, both tubes and ovaries were removed. Because of the uncontrollable oozing of blood from the pelvic floor and wall, the pelvis was packed, and an end of the packing pulled through the rim of cervix into the vagina. The abdomen was closed in layers without drainage. The pathologic report was: tuberculosis of both tubes and right ovary; chronic perioophoritis; perisalpingitis, and fibrosis uteri. The postoperative course was uneventful except for febrile morbidity for 15 days. The patient was discharged on the thirtieth postoperative day.

In 1948, the patient returned to the hospital with symptoms of nerve-root compression. A diagnosis of tuberculosis of the second and third lumbar vertebrae was made by x-ray. A spinal fusion was performed, following which she made an uneventful recovery.

The patient has been followed to date. She is in a good state of health, working as a telephone operator.

A case showing necessity for adequate surgery:

H. J., Case No. 51-7546, a 23-year-old Negro nulligravida, was admitted to the gynecological service on April 27, 1951, complaining of sudden onset of pain around the umbilicus, and radiating to the left lower quadrant. Her last 3 menstrual periods prior to admission had been scanty.

Past history revealed that the patient had a bilateral salpingectomy in another hospital for bilateral pyosalpingitis (confirmed) 6 years previously.

Physical examination showed: temperature 105.6° F., pulse 140; skin dry and hot; the patient having chills; heart and lungs negative. Abdominal examination revealed a healed right paramedian scar, tenderness in both lower quadrants, more in the left; a tender, smooth mass in the left lower quadrant rising 6 cm. above symphysis. Pelvic examination: Cervix conical, firm, and closed; fundus small and displaced to the right; a tender, cystic mass measuring 10 cm. in diameter in the left fornix; induration and a smaller, tender mass in the right fornix. Blood and urine findings were normal. Erythrocyte sedimentation rate was 18 mm. in 40 minutes. Chest x-ray showed normal heart and lungs.

A diagnosis of bilateral ovarian abscess, probably tuberculous in origin, was made. The patient was placed on penicillin and streptomycin therapy. She received 1 Gm. of streptomycin daily for 19 days prior to surgery. Laparotomy was performed on May 18, 1951. The operative findings were: a normal-sized uterus bound down by 2 ovari

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Physical examination showed: temperature 105.6° F., pulse 140; skin dry and hot; the patient having chills; heart and lungs negative. Abdominal examination revealed a healed right paramedian scar, tenderness in both lower quadrants, more in the left; a tender, smooth mass in the left lower quadrant rising 6 cm. above symphysis. Pelvic examination: Cervix conical, firm, and closed; fundus small and displaced to the right; a tender, cystic mass measuring 10 cm. in diameter in the left fornix; induration and a smaller, tender mass in the right fornix. Blood and urine findings were normal. Erythrocyte sedimentation rate was 18 mm. in 40 minutes. Chest x-ray showed normal heart and lungs.

A diagnosis of bilateral ovarian abscess, probably tuberculous in origin, was made. The patient was placed on penicillin and streptomycin therapy. She received 1 Gm. of streptomycin daily for 19 days prior to surgery. Laparotomy was performed on May 18, 1951. The operative findings were: a normal-sized uterus bound down by 2 ovarian

masses, the left measuring 7 by 7 by 5 cm., the right measuring 7 by 5 by 3 cm. The sigmoid was adherent to the posterior wall of the uterus. A total hysterectomy and bilateral oophorectomy were performed. The pathologic report was: Tuberculous abscess of both ovaries.

The patient's postoperative course was uneventful. She was given streptomycin, 1 Gm. daily, from the first postoperative day for 6 weeks. At the time of discharge, the tenth postoperative day, she had no complaints, and her general condition was good. She was seen in the follow-up clinic 7 months after operation. She was still free of symptom, and back at her former occupation.

Streptomycin

As to the value of streptomycin in pelvic tuberculosis, we feel that there have not been enough cases treated and adequately followed to form any definite conclusions. However, considering our experience with the use of antibiotics in chronic gonorrheal adnexal disease, it is safe to say that while streptomycin may help tuberculosis of the tube and endometrium, it will not be effective in the advanced type with masses, induration, and adhesive peritonitis. Streptomycin may be helpful in preventing spread to the osseous and the urinary systems. Some of the cases apparently improved by streptomycin may have had superimposed infection. Sered and Falls[7] feel that streptomycin given 6 to 8 weeks preoperatively seems to make it easier to identify lines of cleavage and to separate dense adhesions. In our experience, streptomycin might have prevented further spread, but did not affect the pathology already present.

The following case illustrates the ineffectiveness of streptomycin in the advanced progressive type of pelvic tuberculosis:

V. F., Case No. 50-6295, a 26-year-old single Negro para 0, gravida i, was admitted to the gynecological service on March 28, 1950, complaining of pain in the lower abdomen, anorexia, weakness, fatigue, and loss of weight, especially during the year prior to admission. During this year, the patient had lost 30 pounds in weight, and was too weak to work. For the 2 months prior to admission she had had night sweats.

Past history revealed that the patient had a criminal abortion in 1947, in the ninth week of gestation. She developed postabortal sepsis and was hospitalized for 3 months in another hospital. Treatment consisted of cervical dilatation and uterine curettage and antibiotics. She admitted frequent and prolonged attacks of head and chest colds. There was no history of any other illness or operation.

Physical examination revealed the following: The lower abdomen was slightly tender and doughy to palpation. There was a mass rising to a level of 6 cm. above the symphysis. Pelvic examination showed the cervix pushed to right and anterior, firm and closed. The fundus was small and pushed to right. The right adnexal area was indurated and tender. There was a tender, elongated, indurated mass in the left adnexal region.

Blood and urine studies were normal. Chest x-ray showed normal heart and lungs.

A diagnosis of possible tuberculous adnexal disease and secondary parametritis was made, and the patient was placed on antibiotics. She was given penicillin, 600,000 units daily, and streptomycin, 1 Gm. daily, both for 1 month. She did not show any improvement. The above drugs were stopped and the patient was placed on aureomycin, 500 mg. four times a day for 1 month, with no improvement. Because of lack of improvement after 2 months of conservative therapy, surgery was deemed advisable.

The gross pathological findings at operation were: The large and small intestines were bound down by dense adhesions to the pelvic viscera. After these adhesions were separated by blunt and sharp dissection, the pelvic structures were visualized. The uterus was enlarged to the size of an 8 weeks' gestation, fixed in position; its surface showed evidence of a fibroplastic exudate. The right tube and ovary formed a mass about 10 cm.

in diameter, which was densely adherent to the posterior layer of the broad ligament and uterus. The left adnexa formed a similar but smaller mass, densely adherent to all the neighboring structures. The base of the broad ligament on both sides was markedly thickened and indurated. The vesicouterine peritoneal fold was thickened and densely adherent. A total hysterectomy and bilateral salpingo-oophorectomy were done. The patient was given 1 Gm. of streptomycin daily for 14 days postoperatively.

Her postoperative course was uneventful. She was discharged on the fourteenth postoperative day in good general condition with no complaints.

The microscopic pathologic report was: tuberculosis of both tubes; of both ovaries with caseation; and of endometrium. The patient was seen 1 year later, still free of symptoms and able to work.

Halbrecht[9] reports 11 of 12 cases of tuberculosis of the endometrium successfully treated with streptomycin. Novak,[10] in his comments on Halbrecht's report, states that streptomycin is definitely indicated in cases of endometrial tuberculosis which are discovered accidentally in women with no clinical evidence of tubal tuberculosis. It is much too early to evaluate its worth in tubal tuberculosis.

We feel that streptomycin and para-aminosalicylic acid is the preferred method of treatment in the ascitic, the tubal, and the uterine types of pelvic tuberculosis. Streptomycin may be of value in the quiescent advance type. We feel that surgery is the only effective treatment for the advanced progressive type of pelvic tuberculosis.

Summary and Conclusions

1. Forty-five cases of pelvic tuberculosis studied and treated at the Harlem Hospital form the basis for the conclusions presented in this paper.

2. The gross pathologic types found were: (a) the ascitic; (b) the tubal; (c) the advanced.

3. We have presented a gross classification of pelvic tuberculosis that will serve a threefold purpose: (a) to provide a knowledge of the gross appearance of pelvic tuberculosis which will enable one to make a tentative diagnosis at the operating table; (b) to give a classification for reporting cases so that there is a common understanding of the type of pelvic tuberculosis under discussion; (c) to afford a basis for evaluating therapy to be used in the different types of pelvic tuberculosis.

4. Pelvic tuberculosis is usually secondary to pulmonary or gastrointestinal tuberculosis.

5. There is a great need for the development of some means of diagnosing pelvic tuberculosis before the case comes to the operating table. In the absence of this, a gross recognition of pelvic tuberculosis is important, because it is only after the abdomen is open that pelvic tuberculosis may be suspected in the majority of cases.

6. Contrary to the usual opinion, the ovaries were involved in 40 per cent of the cases of pelvic tuberculosis in our series.

7. Total hysterectomy with bilateral salpingo-oophorectomy is the treatment of choice in the advanced progressive type of pelvic tuberculosis. Streptomycin promises to be the preferred treatment in the less extensive types of pelvic tuberculosis.

8. The immediate postoperative results in the patients who had extensive surgery were excellent. The patients made a quick and uneventful return to a good general state of health, free of pelvic complaints. Eradication of the pelvic tuberculosis cured the local condition. When systemic tuberculosis is also present, its healing is enhanced by a lessening of the drain on the body's protective forces.

9. Seven patients with advanced progressive pelvic tuberculosis have been treated by ablation surgery. Some of these have been followed as long as 5 years, and have remained free of symptoms and able to carry on productive lives.

10. The fever associated with tuberculosis is usually thought of as being moderate in amount, an afternoon or early evening elevation. However, in several cases we found septic temperatures ranging as high as 104° F. This was especially true in the advanced progressive type. Antibiotics did not affect this temperature. One might presume that the absorption of the toxic products resulting from the breakdown of the body tissue may be a contributing factor.

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A SURVEY OF TWO HUNDRED FIVE GYNECOLOGIC DEATHS, 1938 TO 1950

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SEVERAL years ago a statistical review[1] of ruptured tuboovarian abscess in this hospital indicated that the clinical impression regarding the adequacy of the then current treatment for that condition was erroneous and that lives could be saved by a more radical therapeutic approach. Similarly, Miller[2] in a review of gynecological deaths at Charity Hospital in New Orleans demonstrated the clinical value of such surveys, as did Finn,[3] in a report from the Woman's Clinic of the New York Hospital. Therefore, it seemed worth while to investigate all the deaths from the Gynecologic Service of the University Division of Kings County Hospital between 1938 and 1950, in order to reassess the status of therapy.

Material

During these 13 years, 21,193 patients were admitted to the Gynecologic Service. There were 205 deaths, including those from abortion and ectopic pregnancy, an incidence of 1 to 103 admissions, or 0.97 per cent. While 51.5 per cent of the patients admitted were Negroes and 48.5 per cent were white, a marked deviation from these percentages existed in the deaths. Thus, only 25 per cent of the fatalities from malignant disease occurred in the Negro group and 61 per cent of the deaths from benign causes fell in this category (Fig. 1). This can be explained, in part, by the increased incidence of pelvic inflammatory disease, as well as septic induced abortions among the Negro women admitted to this institution.

Deaths from malignant disease generally occurred at a later age than those from benign causes, the average in the malignant group being in the fifth decade, whereas that in the benign category occurred in the third decade (Fig. 2).

Malignant Disease

More than half of all the deaths, 56 per cent, were due to malignancy of the genital tract, and carcinoma of the cervix accounted for more than half of these (Fig. 3). Although cervical carcinoma is predominantly a disease of the late childbearing period, 13 patients were less than 39 years of age and 16 were over 60 years. The influence of parity is indicated by the fact that 88.9 per cent of the patients who died of carcinoma of the cervix had borne children.

Moderate or profuse vaginal discharge and irregular bleeding were the first indications of genital malignancy in most of these patients. Nevertheless, the first symptoms noted by many of them were pelvic pain, rectal, or urinary difficulties, or abdominal enlargement. There was a tendency to overlook the significance of irregular vaginal bleeding, probably because a large number of the women were in the childbearing age. Symptoms had been present for 6 months to 1 year in 46 per cent of these patients, while 54 per cent were ill for

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over 1 year. As a result 87.3 per cent of the women who died with carcinoma of the cervix were admitted in poor or moribund condition (Fig. 4). Even in the postmenopausal group, where vaginal bleeding should have caused considerable anxiety, it is surprising how few of these patients sought medical advice until 6 months after the onset of the symptoms. Of the 17 women who died of carcinoma of the fundus, 11 had been ill for a year or more before seeking medical aid.

This same lack of early medical care is apparent in those women who died of ovarian carcinoma. Unfortunately, the symptoms of this tumor usually are not manifest until the disease is far advanced. Vague abdominal discomfort, an occasional sign, is too often ignored. Twenty-two of the 26 women who died from ovarian malignancy stated that the first symptom was abdominal enlargement. Even though symptoms in 9 of these patients had been present only from

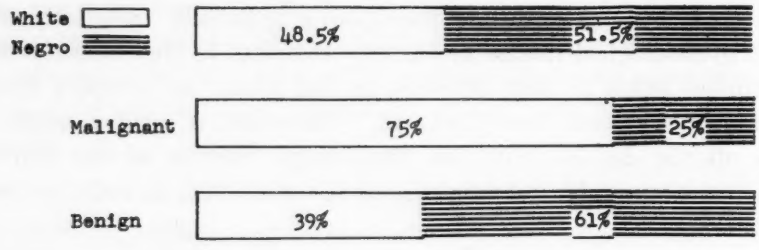

Figure 1. Distribution according to race of 205 gynecologic deaths at Kings County Hospital, University Division, 1938-1950.

1 to 6 months, the lesions were far advanced. The poor general condition of the majority of patients with malignant disease often precludes effective therapy. Thus 61.5 per cent of the women who died with ovarian cancer were admitted in poor or moribund condition (Fig. 4). Very frequently these patients had been treated elsewhere for long periods of time and were sent to municipal institutions for terminal care, so that therapy often had to be purely symptomatic. Accordingly, optimum therapy was given to only 11.1 per cent of the patients with cervical carcinoma; 19.2 per cent of those with ovarian malignancy; and 50 per cent of the women with carcinoma of the vulva (Fig. 5). It is rather depressing to note that not one of the 19 patients who died from malignancy of the body of the uterus had received adequate therapy. By present-day standards, more than half the patients who died from malignancy of the genital tract had received inadequate or purely symptomatic treatment. Failure on the part of patients to obtain medical attention early or to complete their course of treatment was noted in 45.2 per cent of the cases. A review of the histories of the remainder shows, all too often, inadequate therapy and delayed or erroneous diagnosis. Seven patients with carcinoma of the cervix had abnormal bleeding for 1 to 6 years, had consulted physicians, or even had been hospitalized, and yet the diagnosis was not made. An 84-year-old woman had been treated at home for postmenopausal bleeding for 1 year. Four other patients had curettage for postmenopausal bleeding, but vaginal smear or biopsy of the cervix was not done. One of these patients had been in three different institutions and only on the last admission was a biopsy of the cervix taken. Two patients were in the hospital for 2 months prior to cervical biopsy, and in one of these there was a delay of 9 months between the completion of the radium therapy and the start of deep x-ray treatment. Emphasis on careful, routine examination of the cervix, with both biopsy and smear, in spite of normal ap-

pearance, cannot be too strongly made. In our own clinic routine smears and cervical biopsies are performed on all gynecological outpatients, a practice which should become universal.

Three patients had carcinoma of the cervix which was overlooked because of the presence of more obvious pelvic disease. Laparotomy in one of these patients revealed metastatic carcinoma. The other two patients had supravaginal hysterectomies for fibroids, and carcinoma was discovered in the cervical stump 3 and 9 months later. It is reasonable to assume that all 3 patients had carcinoma at the time of laparotomy, but the natural inclination of the operator to remove the obvious abdominal masses resulted in little attention being focused on the cervix. It is now the policy in this institution to perform cervical biopsy and smear prior to abdominal surgery for chronic pelvic disease.

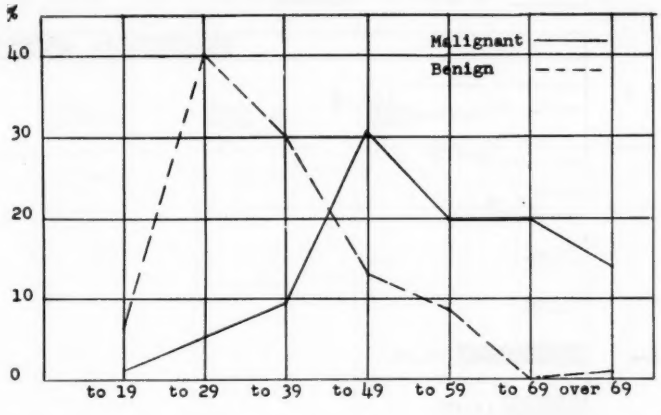

Figure 2. Distribution according to age of 205 gynecologic deaths at Kings County Hospital, University Division, 1938-1950.

Two patients with sarcoma of the uterus, both over 70 years of age, had been observed for several years, but surgery was not performed despite a noted increase in size of the uterus. Both patients were known to have fibroids, and both had been bleeding vaginally. It is obvious that rapid growth of fibromyomas at any age, and continued growth in the postmenopausal period, may be indicative of sarcomatous degeneration.

Incomplete therapy contributed to the death of 5 patients with corpus carcinoma. One individual had had two curettages for postmenopausal bleeding, without a diagnosis having been made. While the diagnosis of pathological material obtained from the fundus, especially during the postmenopausal period, often presents some difficulty, bleeding in this age group, particularly following curettage, should be an indication for more radical therapy. If bleeding recurs after curettage, it is our policy at the present time to perform hysterectomies on postmenopausal patients, regardless of the pathological diagnosis of the removed tissue.

Fibromyomas in patients at or beyond the menopause are treated by some physicians with x-ray. This type of therapy should be reserved only for those who are premenopausal and have had an endometrial biopsy, especially when associated with vaginal bleeding. A 61-year-old woman, 10 years beyond the menopause, received x-ray therapy for an enlarged and bleeding uterus, without preceding biopsy. When bleeding continued, a laparotomy revealed an inoperable carcinoma of the fundus of the uterus.

Therapy, inadequate by present standards, probably hastened the fatal outcome in three patients. One patient died one year after total hysterectomy

for fundal carcinoma without ever having received x-ray treatment. The second patient had radium for the same disease, but received no other treatment. The third received deep x-ray therapy, in addition to radium, but hysterectomy was not done because of the patient's marked obesity.

Ovarian carcinoma is frequently fatal because of the insidious nature of its onset. Cystadenomas of the ovaries are often bilateral, and approximately 50 per cent are malignant, making the extent of operation in younger women somewhat difficult to decide. Menopausal or postmenopausal women should have total extirpation of the pelvic organs. Conservative surgery in 3 patients with ovarian cysts, who were at or beyond the menopause, led to disastrous results.

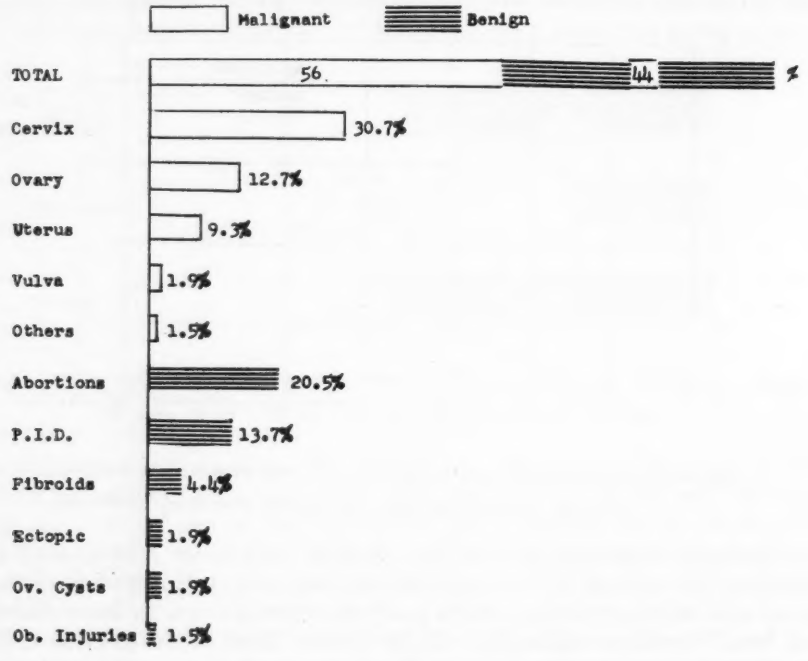

Figure 3. Distribution of pathologic lesions in 205 gynecologic deaths at Kings County Hospital, University Division, 1938-1950.

Benign Disease

As noted in Fig. 1, 61 per cent of women who died from benign disease were Negroes. There was a proportionately higher incidence of deaths from abortion and pelvic inflammatory disease; 70 of the 90 fatalities were due to these two conditions (Fig. 3). It is well known that pelvic inflammatory disease is proportionately greater among Negroes.

Abortion was the single most important cause of death, accounting for 42 cases (Fig. 3). Most of these patients were admitted in poor or moribund condition (Fig. 6). Three of the patients were in shock from hemorrhage, and almost half were febrile on admission. The number of induced abortions is difficult to determine, inasmuch as criminal abortions are reportable by law in this state, so that many patients refuse to give accurate information. However, there is reason to believe that the majority of these cases were either self-induced or induced by abortionists. Five patients had perforations of the uterus when admitted. There should have been a significant reduction in

deaths from abortion in recent years, because of the liberal use of blood transfusions and antibiotics; such an expectation, however, is not borne out statistically (Fig. 7).

As in the case of malignancy, the death rate from abortion would have been lower, if the patients had received medical care sooner. It would appear from Fig. 8 that only 14.2 per cent of these deaths probably could not have been prevented. Eighteen patients waited for 1 week or longer after the onset of vaginal bleeding and fever, prior to seeking medical care; all were eventually admitted in poor or moribund condition.

Generalized peritonitis was present in 5 cases on admission, and autopsy revealed perforation of the uterus with retained placental tissue in all five. One patient was also found to have a perforated bowel. Such accidents are difficult to diagnose, but persistence of peritonitis after adequate antibiotic therapy should create suspicion of perforated viscus, and should lead to exploratory laparotomy.

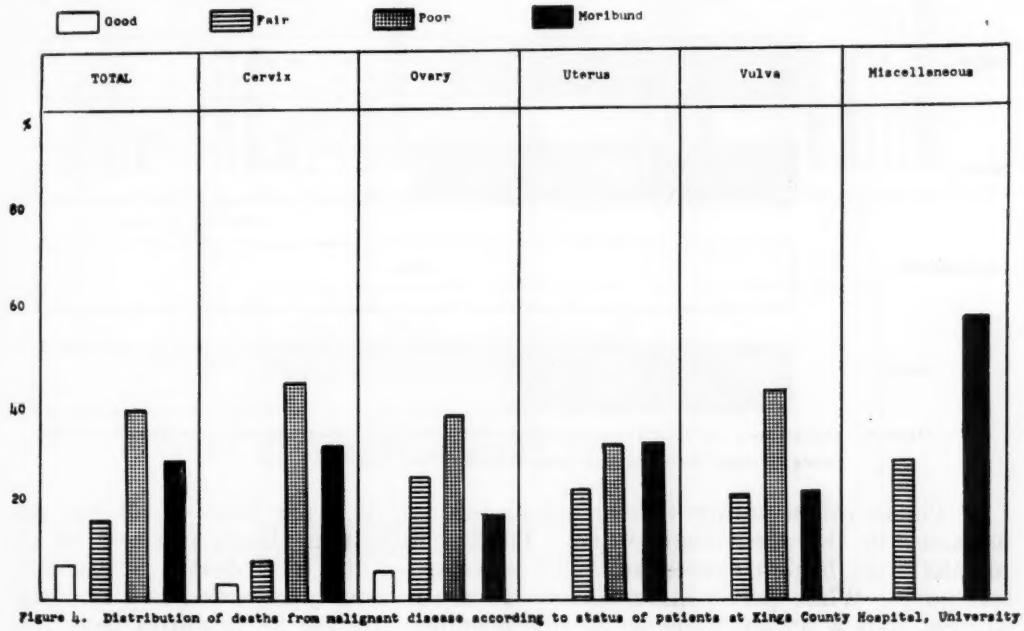

Figure 4. Distribution of deaths from malignant disease according to status of patients at Kings County Hospital, University Division, 1938-1950.

Hemorrhagic shock resulted in 5 abortion deaths. This is rather startling, considering the present-day availability of blood. Despite an admission hemoglobin level of 4 Gm., one patient was given a total of only 1,500 c.c. of blood. On the other hand, overenthusiastic use of blood can be just as dangerous. One patient who received 6,000 c.c. of blood and intravenous fluid during a relatively short period succumbed from acute pulmonary edema. Abortion patients are often admitted in shock from septicemia, due to either anaerobic streptococci or the Welch bacillus. These individuals are extremely difficult to treat, but excessive blood transfusion and intravenous fluid can lead to actual drowning.

It has been our practice to remove retained placental tissue by the finger or sponge forceps, as soon as the patient is able to withstand the procedure. Undue delay in removing placental fragments resulted in the death of 4 patients from hemorrhage and septicemia.

Although parametritis is one of the most frequent complications of infected abortion, tuboovarian abscesses occur more often than is generally as-

sumed. Of the 7 patients with such abscesses, 3 died from rupture of the abscess with generalized peritonitis. The remaining 4 patients recovered after the uterus and adnexa were removed, despite rupture of the abscess in two of these. The treatment for rupture of an adnexal abscess is prompt extirpation of uterus and adnexa.[1]

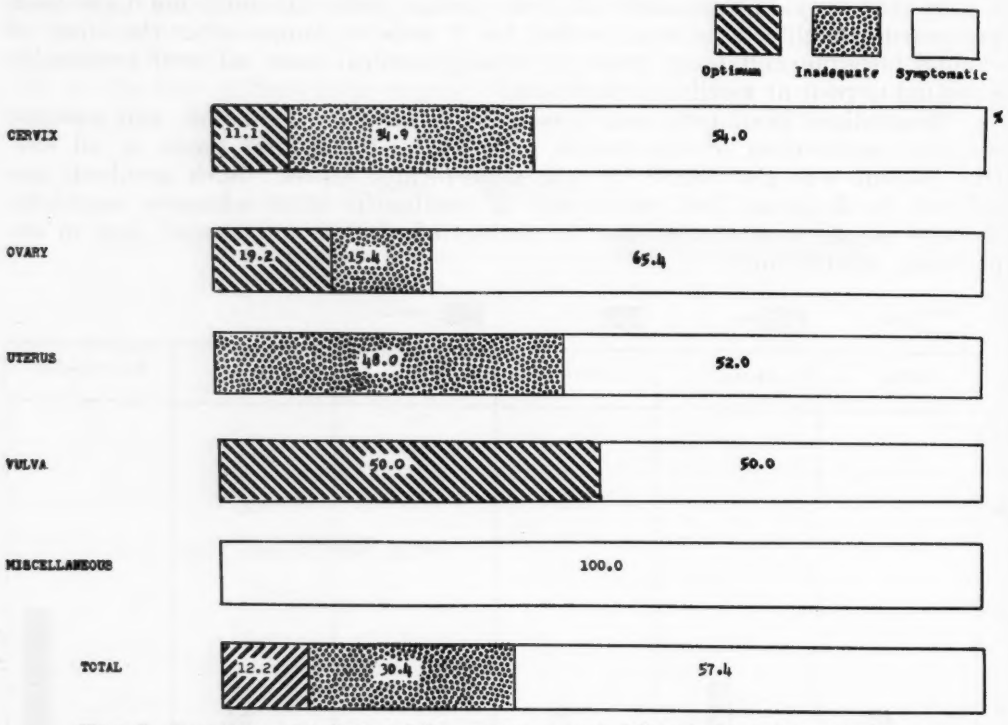

Figure 5. Proportionate distribution of therapeutic measures in 115 deaths from pelvic malignancy at Kings County Hospital, University Division, 1938-1950.

Pelvic inflammatory disease accounted for 39.9 per cent of all the admissions to the gynecologic ward. Thirty-one and one-tenth per cent of all deaths from benign causes, and 13.7 per cent of the total deaths fell in this category. While pelvic inflammatory disease is usually regarded as a nonfatal illness, it is a serious problem in this hospital. Of the 28 fatalities from this disease, 16 patients were admitted with ruptured tuboovarian abscesses and generalized peritonitis. Formerly they were treated conservatively, or by incision and drainage. Since 1947, however, more radical therapy has practically eliminated this cause of death. The histories of several of the remaining 12 patients, who died from pelvic inflammatory disease, are suggestive of ruptured adnexal abscess, although proof is lacking. Inadequate surgery, such as incision and drainage, in patients with unruptured abscesses was a contributing cause of death in pelvic inflammatory disease, and several patients were not operated upon, despite a progressively downhill course.

All the patients admitted for elective surgery, e.g., removal of uterine myomas or repair of obstetric injuries, who subsequently died, were in good or fair condition on admission (Fig. 6). Two of the 9 patients with fibroids died before surgery was done, one from cardiac failure, and the other from a pulmonary embolus. During the period under consideration there were a total of 1,192 hysterectomies for myomas, with 7 fatalities (0.58 per cent), a rate of one in 171 operations. Four patients died from wound evisceration or intestinal

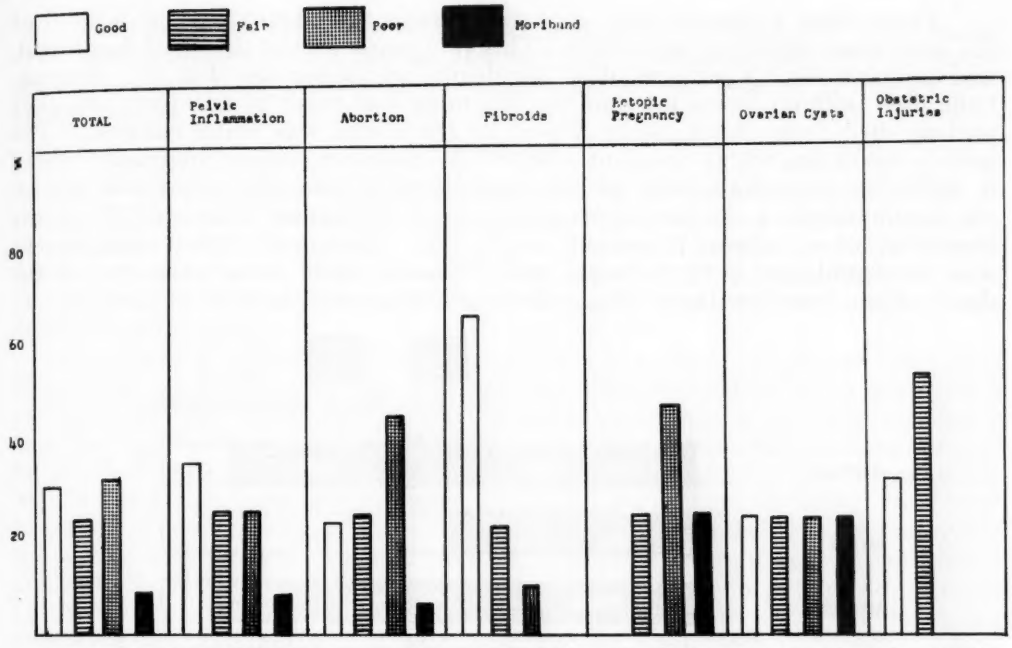

Figure 6. Distribution of deaths from benign disease according to status of patients at Kings County Hospital, University Division, 1938-1950.

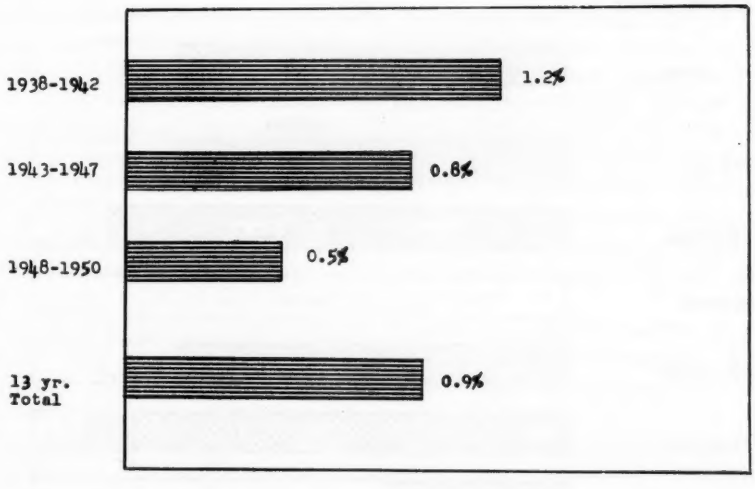

Figure 7. Mortality rate from abortion in the past 13 years at Kings County Hospital, University Division.

obstruction; excessive blood loss, with inadequate blood replacement, contributed to the death of 2 others. During the 13 years covered in this report, a total of 2,362 laparotomies were performed, with 16 eviscerations (0.68 per cent); the only fatalities occurred in the 4 patients operated upon for fibroids. This is a preventable accident, which can be avoided by better preoperative preparation of the patient, careful hemostasis, and better choice of suture material.

In the entire series there was only one anesthetic death.

There were 4 deaths from ruptured ectopic pregnancy, out of a total of 287 such cases admitted since 1938. This represents a mortality of 1.4 per cent, and accounts for 1.9 per cent of all the deaths on the service (Fig. 3). One patient died without operation and the diagnosis was made at autopsy. Another patient died from shock, while a rent of the cornu was being sutured. The serious blood loss which frequently occurs in ruptured ectopic pregnancy makes it advisable to perform only the simplest operative procedure that will control the hemorrhage; a simple hysterectomy may be quicker than repair of the laceration of a ruptured cornual pregnancy. Inadequate blood replacement was responsible for a third death, and too much blood transfusion caused the death of the fourth patient, from pulmonary edema and cardiac failure.

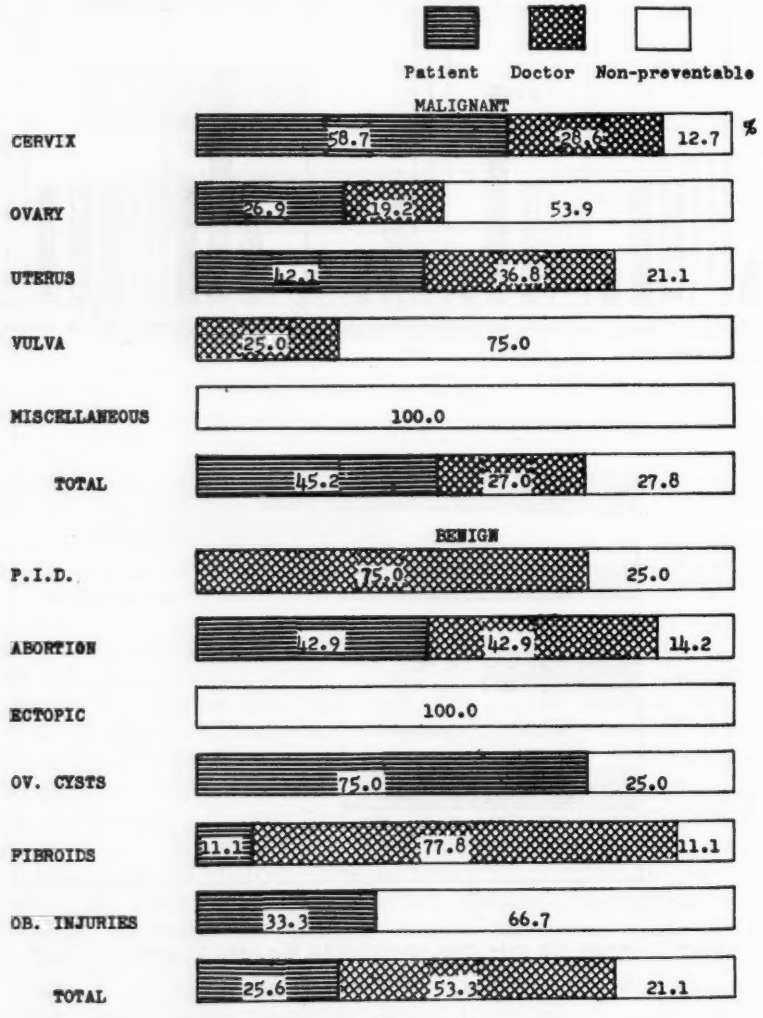

Figure 8. Proportionate distribution of preventability in 205 gynecologic deaths at Kings County Hospital, University Division, 1938-1950.

Four women over the age of 50 died with ovarian cysts. One patient died preoperatively, in cardiac failure, while pneumonia, diabetes, and cardiac failure, respectively, accounted for the 3 postoperative deaths. The diabetic patient had been admitted in acidosis with torsion of the cyst.

Three patients admitted with obstetrical injuries died; one with an incarcerated prolapse of the uterus, and two died postoperatively of pulmonary embolus and coronary occlusion, to account for 1.5 per cent of all the gynecological deaths.

Comment

It is obvious that many gynecologic deaths are nonpreventable. This is especially true in a large city hospital where patients are often admitted late in the course of their disease. And yet, the material herein presented clearly points out areas where improvement could be made. This is particularly so in the field of malignant disease, which accounted for a little over half of the deaths in this report.

Considering carcinoma of the genital tract as a whole, 54 per cent had been ill with symptoms for over one year before being admitted to the hospital; 30.4 per cent had received inadequate medical care, while in 45.2 per cent the neglect had been due to the patient herself. It is perhaps unreasonable to suppose that all of these were salvageable, and yet particularly in respect to carcinoma of the cervix, early diagnosis should result in a high percentage of cures. Not only is cancer education necessary for the laity, but proper training is necessary for the doctor and medical student. Within the last year routine cervical biopsy and smears are taken on all patients in the gynecological outpatient department of this clinic. Medical students are taught that this is part of a thorough gynecological examination. This procedure has been most impressive, for it has resulted in the finding of a 2 per cent incidence of carcinoma, many in cervices which would be by-passed as grossly normal.

The vast majority of deaths from benign disease were accounted for by abortion and pelvic inflammatory disease, 20.5 per cent being due to the former and 13.7 per cent to the latter. As has been stated before, the law in New York making criminal abortions reportable, and the attendant furor which accompanies such reporting, tend to make the patient conceal this factor. Nevertheless, a preponderance of the seriously ill and neglected abortion patients must fall in this category. Of necessity, because of such numbers, the majority of these cases have been curetted within 24 hours of admission. The results, on the whole, have been good, with deaths resulting from overwhelming infection, neglect on the part of the patient, and unrecognized criminal perforation of the uterus. The failure to reduce death rates from abortions with all the modern methods of therapy now available is disappointing.

Rupture of the tuboovarian abscess, despite its general rarity, is of common occurrence in this institution, and accounted for approximately one-third of the deaths from benign disease. Since 1947 complete and radical surgery in these cases has practically eliminated this cause of death.

The fatalities among the patients admitted for elective surgery point up the importance of thorough history, physical, and laboratory examination, as well as thorough preoperative preparation of the patient.

Summary

1. Two hundred five consecutive gynecologic deaths over a thirteen-year period were reviewed.

2. Malignancy of the genital tract accounted for 56 per cent of all the deaths.

3. Although 51.5 per cent of the patients admitted to the gynecologic ward were Negroes, they accounted for only 25 per cent of the deaths from malignant disease, and for 61 per cent of the deaths from benign disease. The explanation

lies in the higher incidence of septic abortion and pelvic inflammatory disease among the Negro women admitted to this institution.

4. Carcinoma of the cervix was responsible for more than half the deaths from malignant disease. Routine vaginal smear and biopsy of the cervix probably would sharply reduce the incidence of deaths from this cause.

5. Earlier treatment in the malignant disease group can be achieved through better education of the laity and medical profession. This lack is indicated by the large number of patients admitted to the hospital in poor or moribund condition, and the inadequate medical care given to 30.4 per cent of the patients.

6. The average age at death from malignancy of the genital tract was in the fifth decade, whereas that from benign disease occurred in the third decade.

7. Abortion and pelvic inflammatory disease were responsible for 20.5 per cent and 13.7 per cent, respectively, of the deaths from benign disease.

8. While there has been no significant decline in the death rate from abortion, that from pelvic inflammatory disease has been virtually eliminated. In large measure this decline has been due to antibiotics and more radical surgery for the latter condition.

9. Concealment of criminal induction by the patient is partially responsible for the continued high mortality rate from abortion, despite antibiotics and blood transfusion.

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451 CLARKSON AVENUE

Rh COUNTERSENSITIZATION*

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STIMULATED by Unger's[1] report on the apparent efficacy of bacterial vaccines in the prevention of sensitization to the Rh factor, an Rh Countersensitization Clinic was established at the United States Public Health Service Hospital, Staten Island, in January, 1950. All pregnant women found to be negative for the Rh_0 and rh′ factor when their erythrocytes are examined are referred to this clinic. The rationale of this clinic is based on observations made during 150 years.

As knowledge and information have increased concerning the system of Rh factors and the reciprocal Hr factors, it has become apparent that they operate within the laws governing antigen-antibody phenomena and that they are, in fact, antigens.[2]

Among the antigen-antibody phenomena there is found a series of occurrences that have been variously described as interference phenomena, competition of antigens, sparing effect, cell blockade, and blocking of antigen-antibody union. The clinical observation of the interference of one antigen with the antigenicity of another was first noted and recorded in 1804, when Jenner[3] reported the modification or the elimination of vaccinia lesions in those patients who had recently had a herpetic infection with lesions.

Investigators in virus research[4] have noted many instances of the reduction or the elimination of the antigenicity of one virus in the presence of another specific virus; however, for different viruses, different specific criteria must be met. Two viruses may be administered simultaneously to a host susceptible to both of them and the host may respond to only one.[5] With other viruses, there is a factor of timing, and in order to prevent the response to a specific virus, the interfering virus must be administered first and a suitable time interval allowed to elapse.[6]

In the cross immunity developed by antigenically related and unrelated bacteria, this time lapse is of great importance for the cell blockade to be formed. The superior degree of immunization obtained with diphtheria[7] toxoid in type A individuals as contrasted with type B individuals is a classic example of the competition among antigens. There is "A" substance present in the toxoid to which the type B individual may react, but to which the type A individual cannot react. In these cases, the type A individual receives only

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one antigen to which he may respond, and develops a higher titer than the type B individual who responds to two antigens. While some bacterial antigens function as synergists when simultaneously administered,[8] the majority of these antigens will appear to compete with each other when given together. In this type of response, when two antigens are given simultaneously, antibodies will be made to both antigens but in a lower titer than if given singly.[9]

The role of steroid hormones in this field of antigen-antibody response is not conclusive, but there is good evidence to show that at least some of these substances exert a marked influence over hypersensitivity manifestations[10] and that they may also alter the antigen-antibody interaction.[11] It has been shown that the administration of cortisone and ACTH has interrupted the allergic manifestations to streptococcal infections,[12] reversed a tuberculin reaction,[13] and in similar fashion has prevented the union of antigen and antibody.

The beneficial effects of some antibiotics may be bracketed with these phenomena in those cases in which the organismal multiplication is stopped without direct destruction of the organism.[14] This action has the single effect of either minimizing or preventing the formation of antibodies. There may be additional logic to the inclusion of antibiosis with these phenomena when the modus operandi for the entire system is considered.

The common factor in the preceding series of observations, with its multiple facets, is the restriction, alteration, or elimination of antigenicity. While each individual group is subject to many theories, it may well be that there is but a single plausible theory capable of explaining all of these occurrences, including the results obtained in our series.

The action of vaccines and the role of hormones and antibiotics cannot be explained through theories hypothesizing interference via inflammatory tissue alteration and increases in noxious metabolites.[15] A blockade of the reticuloendothelial system such as occurs with carbon particles cannot be ascribed to antigens when the occasional synergism among antigens is remembered. Dual infections plus antigenic synergism eliminate the receptor destruction theory hypothesized for hemagglutination.[16]

The sole theory which appears to be applicable to all occasions has aptly been termed the "key enzyme" theory.[17] This theory concerns itself with the vital obligatory role of enzymes in organismal respiration, metabolism, and propagation. It is applicable when enzyme systems are considered as catalytic agents for the activation and conversion of steroids, with the result that those enzymes are no longer immediately available for use. Antibiotics are included because of their ability to immobilize many enzymes necessary to organismal multiplication. Utilizing this theory, the occurrence of dual infection and interference is simultaneously explained. In the first instance different enzymatic pathways are used, while, in the latter, certain enzymes are used by both organisms, and competition is established. In addition to the explanation for the reduction of antigenicity, this theory will also account for the intervention in the antigen-antibody union. Antibodies frequently demand

the addition of other factors in order to unite with their antigens and these factors may be enzymes utilized by the steroids. Antigens, in the form of bacterial or viral vaccines, follow the same competitive pattern as their living source and appear to retain the ability to fix the same enzymes that are utilized by the living organism. Therefore, these vaccines may and do interfere with living organisms or other antigens. This "key enzyme" theory can account for the results set forth in this paper if all antigens, regardless of source, require the presence of a specific enzyme during the production of antibodies.

The bacterial vaccine therapy was originally suggested by Weiner,[18] in 1944, as a benign method of determining the practicality of the theory of competition among antigens. Before placing pregnant women on a regime of bacterial vaccines, Unger[1] in this country and van Loghem[19] in Holland tested the procedure in male patients. The production of high titer diagnostic sera by multiple injections of known Rh-positive erythrocytes into male volunteers has given a cumulative sensitization incidence of 54.4 per cent[20] and this has been used as a basis for comparison. Using entirely different methods of "timing" and different dosages of both vaccines and Rh-positive erythrocytes, these investigators demonstrated a sharp reduction in the incidence of sensitization in their series of volunteers.

Unger, following Weiner's exact method of production of high titer sera, but with the addition of vaccine, obtained sensitization in 14 per cent. Van Loghem, using a technique that varied in all respects, obtained an incidence of 21 per cent. If this reduction in sensitization could be applied to the much lower incidence in pregnant women, bacterial vaccine therapy would provide a strong preventive weapon in combating erythroblastosis fetalis.

The procedure at our clinic is similar to that used by Unger and consists of the initiation of vaccine therapy as soon as the pregnant woman is referred, then the investigation of the sensitization status, and finally the establishment of the incompatibility of the mating by Rh_0 and rh′ determinations in the father. The establishment of the specific therapy in advance of confirmation of the Rh incompatibility is necessary because of the nature of the beneficiaries at this institution. The husband frequently is located at a great distance from the hospital, due to his active military status. This vaccine therapy consists of a course of six weekly injections of typhoid vaccine, then six weekly injections of pertussis vaccine. This cycle is continued, with an increase in dosage at every change, until labor ensues. Table I illustrates the format of the vaccine record and incompatibility summary used in our clinic.

Sensitization to the Rh antigens is determined monthly until the thirty-fourth week of gestation and then every two weeks until parturition occurs. A qualitative determination is done, using saline, albumin plasma, and Coombs' antiserum globulin as the testing procedures. When sensitization has occurred, a quantitative determination is done, again using standard methods. The titer is determined both in our laboratory and the Blood Transfusion Association in New York City.

At the time of delivery ABO and Rh determinations are performed on the infant, as well as an erythroblast count, a red cell count, white cell count, and

a hemoglobin determination. Circulating Rh antibodies are tested for in the mother and infant at the time of delivery and in addition the antibody titer for immunization against typhoid and pertussis is determined in the infant. Currently, 229 infants of incompatible matings have been delivered after maternal treatment in our clinic, and 35 women with incompatible matings are now under therapy. Eighteen Rh-negative infants have been delivered but these patients are not included in this paper; nor are the patients who have not delivered.

Eight patients were found to be sensitized before therapy was begun and their course is summarized in Fig. 1. Observation of only 8 sensitized patients renders any occurrence interesting, but a trend should not be forecast. However, it is of interest to note that a well-established titer with a suggestive previous history reverted to negativity in 2 cases. The short duration of circulating Rh antibodies is very unusual[21]; however, similar titers were obtained by both testing laboratories. The 4 liveborn erythroblastotic infants were severely involved and all were treated with ACTH or cortisone. Two infants received ACTH with a single transfusion to correct an existing anemia and they both made rapid and complete recoveries. One infant showed dramatic improvement with cortisone and did not receive additional therapy, while the remaining infant received ACTH and cortisone, and an exchange transfusion was unsuccessfully attempted. These latter two cases as well as the case of hydrops fetalis have previously been reported.[11] The occurrence of 6 cases of

TABLE I

Rh COUNTERSENSITIZATION CLINIC

Patient— Rh negative
Type _____
Husband—Rh _____
Type _____

Gravida_____ Para_____
Previous pregnancies
_____
_____

TYPHOID *250 Million Organisms*	PERTUSSIS *10,000 Million Organisms*	TYPHOID *500 Million Organisms*
1st Week _____	7th Week _____	13th Week _____
2nd Week _____	8th Week _____	14th Week _____
3rd Week _____	9th Week _____	15th Week _____
4th Week _____	10th Week _____	16th Week _____
5th Week _____	11th Week _____	17th Week _____
6th Week _____	12th Week _____	18th Week _____
PERTUSSIS *40,000 Million Organisms*	TYPHOID *1,000 Million Organisms*	PERTUSSIS *80,000 Million Organisms*
19th Week _____	25th Week _____	31st Week _____
20th Week _____	26th Week _____	32nd Week _____
21st Week _____	27th Week _____	33rd Week _____
22nd Week _____	28th Week _____	34th Week _____
23rd Week _____	29th Week _____	35th Week _____
24th Week _____	30th Week _____	36th Week _____
ANTIBODY TITERS		CORD BLOOD
12th Week _____	32nd Week _____	Rh _____
16th Week _____	34th Week _____	Type _____
20th Week _____	36th Week _____	Rh Antibodies _____
24th Week _____	38th Week _____	Smear _____
28th Week _____	Delivery _____	Count _____

Name: Last First Register No.

erythroblastosis in the 8 sensitized cases in this series and similar results in other series indicates that this regime is of preventive rather than therapeutic value.

The course of the remaining 203 patients, not sensitized at the onset of therapy, is summarized in Table II. With these nonsensitized mothers who delivered Rh-positive infants, not a single case of sensitization during therapy occurred. This observation is of further importance when it is realized that 10 patients have delivered twice while under therapy, all of them as primigravidas and again as multigravidas, without sensitization. Two patients have delivered three times under this regime and still remained nonsensitized.

While statistics vary,[22] the average figure listed for the incidence of erythroblastosis is 1 in every 200 pregnancies. For Rh-negative mothers, the figure is given as 1 case in 26 pregnancies. Finally, the important incidence of 1 case of erythroblastosis in every 22 Rh-incompatible matings is felt to be average. Unfortunately, statistics for those cases that fulfill all the present criteria for sensitization, namely, only incompatible matings that produce Rh_0 or rh′ positive infants, are not available. However, this incidence must necessarily be higher, possibly as high as 1 case in 16 pregnancies. The relative rarity of erythroblastotic incidence has been adequately covered in many previous articles.

Applying these statistics to our series of 203 women who were not sensitized when first seen in our clinic, 12 cases of erythroblastosis might have been

PATIENTS SENSITIZED AT ONSET OF THERAPY

PATIENT	GRAVA	HISTORY	TITER	GESTATION IN WEEKS 16:20:24:28:32:34:36:38:D	INFANT
M.F.	III	3rd child neonatal death	64, 16, 4		Normal Rh positive female
H.C.	VI	5th child jaundiced and transfused	32, 8, 2		Normal Rh positive male
A.M.	III	No history of previous difficulty	64, 16, 4		Erythroblastotic female - ACTH and blood - survived
P.G.	III	No history of previous difficulty	64, 16, 4		Erythroblastotic male - ACTH and blood - survived
M.W.	IV	3rd child jaundiced and transfused	32, 8, 2		Erythroblastotic male - Cortisone - survived
A.K.	II	No history of previous difficulty	256, 64, 16		Erythroblastotic female - ACTH and Cortisone - died
R.A.	III	No history of previous difficulty	256, 64, 16		Erythroblastotic Stillborn
M.V.	IV	3rd child - died of erythroblastosis	1024, 256, 64		Hydrops Fetalis

Fig. 1.

TABLE II. PATIENTS NOT SENSITIZED AT ONSET OF THERAPY

	NUMBER TREATED	NUMBER SENSITIZED	NORMAL INFANTS	ERYTHROBLASTOTIC* INFANTS
Present Study.—				
Primiparas	82	0	82	0
Multiparas	121	0	121	0
Unger's Study.†—				
Primiparas	40	0	40	0
Multiparas	81	2	79	2
Unger's Study.‡—				
Primiparas	49	0	49	0
Multiparas	144	2	142	2
Total	517	4	513	4

*All of the affected infants recovered.

†Published in *Proceedings of the International Society of Hematologists, Third International Congress,* Cambridge, 1950.

‡Personal communication.

predicted. If we include those patients studied by Unger, 32 cases of erythroblastosis would be expected. Instead of 32 cases of erythroblastosis, there were only 4 cases in the combined series of nonsensitized mothers.

Considering the incidence of sensitization in contrast to erythroblastosis, among those patients who were not sensitized at the onset of therapy the results are even more significant. In the usual series of untreated patients there are many cases of sensitized mothers who produce normal infants. In this combined series of cases the only patients who became sensitized were those who became sufficiently sensitized to produce erythroblastotic infants. In view of our observation of 2 cases with antibodies which persisted for only a short duration, it may well be that these 4 patients had actually been sensitized previously and reverted to negativity. If this were the case, a priming effect would have been exerted and a hypersensitive state would have existed with results similar to the results in cases with known sensitization.

Summary

While the series of patients presented in this paper is not large, it is felt that the results are too significant to be disregarded. There was a sharp reduction in the expected number of erythroblastotic infants in this series and this reduction is attributed to the use of bacterial vaccines by our Rh Countersensitization Clinic. The efficacy of this bacterial vaccine therapy can be accounted for by applying the "key enzyme" theory as the explanation for competition among antigens.

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THE CAUSE OF THE BLOOD AND VASCULAR ALTERATIONS OF NORMAL PREGNANCY AND PRE-ECLAMPSIA-ECLAMPSIA

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DEFINITE alterations in the maternal blood and vascular system occur during the course of normal and toxemic gestation.[1, 2, 3] Extensive investigation has established that these changes, while varying in degree, follow a pattern. The purpose of this paper is to advance a theory that during pregnancy there are two anatomical conditions in operation at the placental site which may explain these changes. The first is the presence of a modified arteriovenous fistula. The second is the presence of resistance to the flow of maternal blood through this fistula.

Modified Arteriovenous Fistula

The concept that a modified arteriovenous fistula is present at the placental site is not new.[4] Anatomical dissection[2, 5] and vascular injection studies[6, 7] employing various agents have clarified the maternal uteroplacental circulation. The arterial supply is derived from two sources, principally the uterine and to a lesser extent the ovarian arteries. As the uterine arteries enter the uterine wall they divide into convoluted branches which, by anastomosing freely with each other as well as with branches from the ovarian arteries, form an arcuate system which encompasses the uterus. From this system radial arteries extend to nourish the uterine muscle and endometrium. As the branches extend toward the uterine cavity, they divide into basal arteries, which nourish the inner layer of the uterine musculature and basal part of the endometrium, and endometrial arteries, which are coiled and nourish the remainder of the endometrium. From the dense vascular bed in the endometrium and myometrium the blood is returned by thin-walled veins, which form an irregular anastomosing net with sinusoidal enlargements at all levels, and pursue a course the reverse of that of the arteries. At the placental site the vascular pattern is more intense and modified. Here the radial arteries are extremely convoluted and coiled as they penetrate the decidua basalis and open into the intervillous space through the maternal cotyledons. The arterial blood flows through the intervillous space toward the subchorionic lake under the fetal placental surface and drains as venous blood into the marginal sinuses, from which it is returned to the uterine veins. The intervillous spaces are not lined by endothelial cells but rather by fetal tissue.[2] Thus the human placenta has been aptly described as being of the hemochorial villous type,[8] its site of implantation being characterized by the maternal arterial vessels communicating directly with the venous channels through a large blood lake into which the chorionic villi protrude to achieve fetomaternal exchange.

When an arteriovenous fistula is present in the body the following alterations in the blood and vascular system are found[9, 10]: a decrease in systolic and diastolic blood pressure with an increase in pulse pressure; an increase in the pulse rate and cardiac output; an increase in blood volume; and an elevation of the venous pressure beyond the shunt. Similar changes occur in the maternal organism in response to pregnancy.[1, 2, 4, 11] They are first demonstrable in the

first trimester and become more accentuated as pregnancy progresses until the latter part of gestation. In view of the anatomical characteristics of the human placenta and the remarkable similarity of the blood and vascular pattern during pregnancy and an arteriovenous fistula anywhere in the body, it is felt there is justification for Burwell's contention that a modified arteriovenous fistula not only is present at the placental site but that it is of etiological significance.

Originally it was believed that these same alterations continued until term, but it has now been established that during the latter weeks of gestation the blood and vascular pictures change.[1, 2, 3, 13-17] It is the author's contention that while the alterations of the greater part of pregnancy arise from the presence of a modified arteriovenous fistula at the placental site, those of late gestation are due to resistance in the shunt and that the latter is perfectly consistent with the former when one considers the growth and development of the placenta.

Placental Resistance

As previously stated, the human placenta is of the hemochorial villous type. Each villus arises from the chorionic membrane as a single stem which descends from the chorionic plate to the decidua basalis. These anchoring villi give origin to branches which in turn branch and rebranch, developing an arborescent form, the complexity of which increases with advancing placental growth.[2] They float in the blood-filled intervillous space in a chandelier-like pattern.[7] During the latter part of pregnancy the terminal villi anastomose with each other[18] and form a dense meshwork of chorionic branching through which the maternal blood must flow in its passage from the spiral arterioles in the decidua basalis to the subchorionic lake. Dodds[19] and Dees-Mattingly[20] have calculated that at term the total end-to-end length of the chorionic villi is 11.4 miles with a total surface area of 70 to 120 square feet. This is over four times the estimated total capillary bed of both kidneys (1.56 to 2 square meters).[5, 21] When one considers this tremendous surface area and mass of microscopic branching projecting into the maternal blood stream, it can be seen that the evolution of the human placenta in an attempt to obtain a large absorptive surface has resulted in a marked resistance to the flow of maternal blood. In addition, as pregnancy advances the intervillous space separating the artery and the vein increases from an obviously negligible capacity to one of 90 to 330 c.c. of maternal blood at term.[2] This resistance at the placental site is further augmented in that during the last trimester the uterine wall is increased by a process of stretching rather than muscle growth with narrowing of the maternal blood vessels.

It is the contention of this presentation that the increasing tortuosity of the chorionic villi augmented by the separation of the artery from the vein by the growing intervillous space and by narrowing of the maternal vessels incidental to uterine stretching not only obliterates the modified arteriovenous fistula, but as an area of resistance initiates its own blood and vascular alterations.

Physiological experiments[9] have shown that an increase in peripheral resistance to the flow of blood through the vascular tree results in the following compensatory mechanisms aimed at maintaining circulatory equilibrium: an elevation of the systolic and diastolic blood pressure with the diastolic being primarily affected; an acceleration of the heart rate; a concentration of the circulating blood volume; and constriction of blood-vessel walls. Hare and Karn[22] have shown that in the latter weeks of gestation there is a rise in the systolic and diastolic pressure from their mid-gestational lows toward their nonpregnant values and that the diastolic pressure is primarily affected with a resultant decrease in pulse pressure. Stander and Cadden[23] have shown that there is an acceleration of the pulse rate in normal pregnancy which increases toward

term. Determinations of the circulating blood volume at intervals during the course of pregnancy[14-17, 24] have revealed that there is a significant rise (attributable to the fistula, as previously mentioned) up to approximately the thirty-fourth week but that from then on to parturition there is a substantial decrease. Is this not in truth hemoconcentration? Vasospasm has not been clinically demonstrated during normal pregnancy but experimentation with cold pressor tests has shown that many women are hyperreactors with a latent vasomotor instability. The frequent and profound fluctuations in blood pressure of pregnant women under spinal anesthesia are further suggestive evidence of its presence.

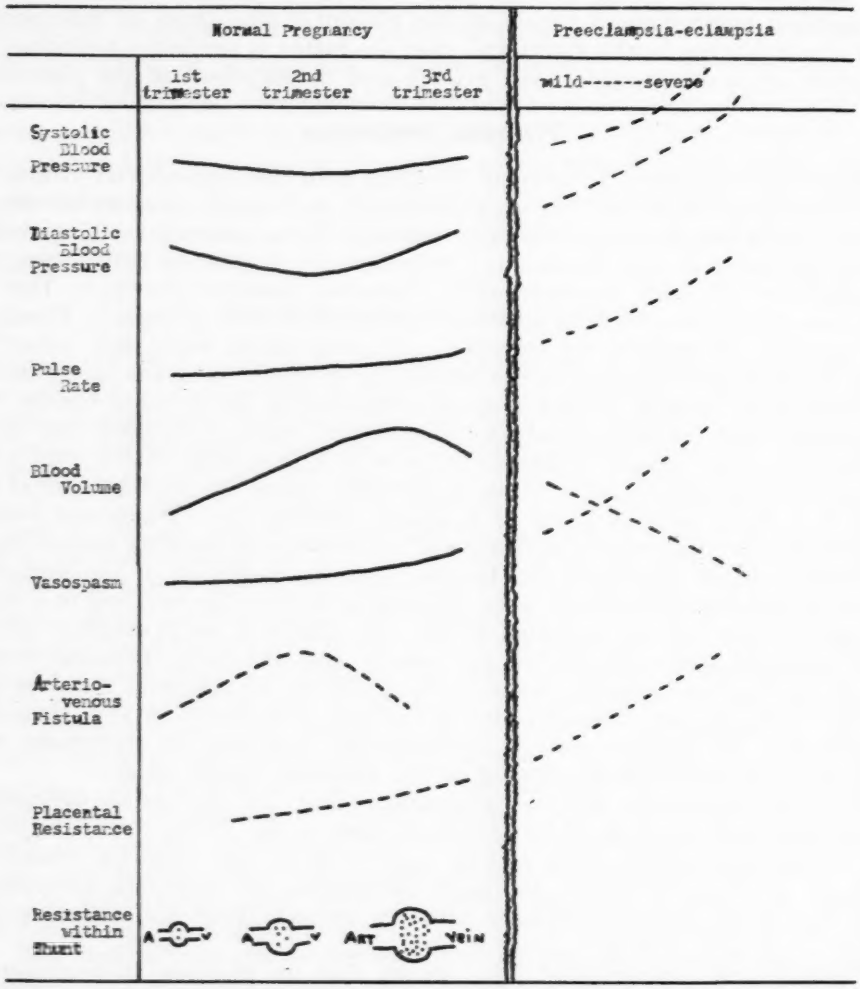

Fig. 1.

It is felt that an area of resistance at the placental site is shown not only by the anatomical studies and the blood and vascular alterations mentioned but also by the observations that at term the flow of maternal blood through the placental site is practically stagnant,[13] and that in placental aortography there is pooling of dye at the placental site.

In Fig. 1 these findings are graphically depicted. The systolic blood pressure begins to drop during the first trimester and continues to decline until

mid-gestation following which there is a rise toward the nongravid state. The diastolic blood pressure follows a similar curve. However, during early gestation its fall is proportionately greater than that of the systolic and during late gestation its rise is proportionally greater with a resultant increased pulse pressure at mid-gestation and a decreased pulse pressure at term. The blood volume begins to rise during early gestation, reaches its peak at about the thirty-fourth week and then decreases toward term. The pulse increases slowly during all of gestation but shows the greatest relative increase during the last few weeks. Vasospasm while not definitely proved is felt by this investigator to begin around the third or fourth month and to increase as pregnancy approaches term. The influence of the modified arteriovenous fistula and the resistance of the placental site is depicted by the broken lines and diagrammatic drawing in Fig. 1.

In summary the blood and vascular changes in early pregnancy are due to the presence of a modified arteriovenous fistula and as pregnancy advances the resistance to the flow of maternal blood across the fistula increases to such an extent that it not only physiologically obliterates the shunt but initiates its own compensatory blood and vascular alterations.

In response to an area of resistance in the body the compensatory mechanisms that are initiated to overcome its effect work as a whole rather than independently, and each has an effect on the others so that a chain reaction is initiated. Peripheral resistance causes vascular spasm; this in turn increases the volume of circulating blood by diminishing the size of the vascular bed. This increase in blood volume throws a greater load on the heart and tachycardia results. Hemoconcentration occurs to lighten the cardiac load, but hemoconcentration and vasospasm also offer increased resistance so that the blood pressure and cardiac rate must increase to maintain circulatory efficiency. Thus a cycle is initiated the extent of which is directly proportional to the resistance at the placental site; that is, the greater the resistance, the more intense the response. That there is a wide individual variation in the blood and vascular alterations of late gestation is an accepted fact.

When the resistance at the placental site and the cycle it initiates produce blood and vascular changes within physiological limits, the result is normal pregnancy. But what if the resistance were greater? Would not the blood and vascular alterations be accentuated to hypertension (a rise in the systolic and diastolic blood pressure with the latter primarily affected, a decrease in pulse pressure), tachycardia, hemoconcentration, and vasospasm, and would not the clinical findings be directly proportional to the degree of resistance? Fig. 1 shows this accentuation.

Is this not the picture of pre-eclampsia-eclampsia?

Pre-eclampsia-Eclampsia

It is not the contention of this article that the blood and vascular picture in pre-eclampsia-eclampsia is necessarily dependent upon the number and/or size of the chorionic villi, but rather that it is dependent upon the extent of blockage this resisting mass offers to the flow of maternal blood across the placental site.

It is well known that the incidence of pre-eclampsia-eclampsia increases as pregnancy approaches term, that it occurs more often in association with multiple pregnancy, polyhydramnios, hydrops fetalis, hydatidiform mole, diabetes mellitus, hypertension, and cardiovascular-renal disease, and that it is more prevalent in primigravidas than multigravidas.

It is felt that a more effective resistance can be demonstrated in each of these predisposing factors due to their inherent placental uterine characteristics.

Effect of Uterine Stretching

The work of Earn and Nicholson[7] on placental circulation, confirming that of Spanner, has shown that only the major anchoring villi from the fetal surface transverse the subchorionic lake, that the terminal villi do not extend into this area, and that in utero the placental thickness may be two to three times that found at delivery. It is apparent that any decrease in the size of the subchorionic sector of the intervillous space would force the chorionic villi into more intimate contact with the maternal blood and result in more effective resistance.

The uterine musculature increases during the first few months of gestation by a process of hyperplasia and hypertrophy of the muscle cells.[13] At about the fourth month the placenta is attached to about one-half of the area of the uterine wall.[3] During the last half of gestation the increase in uterine size is due to stretching of the muscle fibers rather than to muscle growth.[25] During this period placental growth does not keep pace with the degree of myometrial stretching so that at term the placenta covers only one-fourth to one-third of the uterine expanse. It follows that concomitant with this stretching of the uterine wall the attached placenta is attentuated, resulting in compression of the intervillous space. During this same period the resisting surface area of the placental mass within this space is approaching its peak due to the arborescence of the chorionic tree. In other words, as pregnancy approaches term, the flow of maternal blood across the placental site meets its optimum resisting force and encounters it more directly due to attentuation of the intervillous space. Uterine stretching acts as the mechanism causing the chorionic villi to be confined within a more compressed space so that their effective blockage to the flow of maternal blood is more efficient. It follows that conditions of pregnancy which produce an overdistention of the uterus should augment this process. In polyhydramnios and multiple pregnancy the blood and vascular alterations frequently extend into the abnormal levels of pre-eclampsia-eclampsia.

Effect of Placental Pattern

When the placental pattern in hydatidiform mole and severe cases of Rh incompatibility are viewed microscopically, the chorionic villi due to cystic degeneration or edema of the stroma are enlarged and the intervillous space diminished so that the free flow of maternal blood across the placental site is effectively retarded. In addition, in these instances the placental mass is larger.

Effect of Pressure

Labor is characterized by an increase in intrauterine pressure incident to uterine contraction with compression of the intervillous space. In the primipara the placental site is more compressed than in the multipara due to a tauter uterine and a firmer abdominal musculature. The increased resistance due to this tamponade of the intervillous space is further augmented by the smaller vessels found in the primiparous uterus as shown by Beker.[26]

Effect of Vascularity

The blood and vascular picture due to resistance at the placental site may be altered in the following manner. As maternal blood enters the uterine circulation, it has two courses of flow—one, to the placental site, and two, to the remainder of the uterine musculature not covered by the placenta. Gillespie[25] has postulated that the tortuous myometrial blood vessels uncoil as the uterus undergoes stretching in the latter part of gestation. Thus the resistance to the

flow of maternal blood through the myometrial blood vessels is decreasing while the resistance at the placental site due to the chorionic arborescence is increasing. It follows that if the resistance to the flow of maternal blood across the placental site were too great, part of the blood could then follow the course of least resistance, by-pass the placental sector, and flow on through the myometrial course. In this way the effect of the resistance at the placental site would be proportionally offset, and the blood and vascular alterations less accentuated. However, this would also mean that the oxygen supply to the placenta would be partially decreased, and the chorionic villi farthest from the source of supply would undergo degeneration, their resisting surface area be destroyed, and thus the total placental resistance lessened. When the resistance in the placental circulation falls below that in the myometrial circulation, more blood would again flow to the placenta. This process could repeat itself many times during pregnancy without affecting any appreciable change in the blood and vascular picture.

An increased vascularity of the myometrium would facilitate this process. In multiparas this increase is found and probably accounts for the greater senescence in many of their placentas. Estrogenic substances increase the vascularity of the uterus.[2] It has been shown that the administration of stilbestrol during pregnancy to primiparas diminishes the anticipated incidence of pre-eclampsia-eclampsia[27] and that the placentas of the patients so treated revealed a greater senescence than those of the untreated.[28]

Effect of Compensatory Powers

In diabetes mellitus, hypertension, and cardiovascular-renal diseases the vascular system is already damaged. The compensatory powers of these patients are already under strain, and the additional load incident to the growing placenta results in further derangement of their circulatory equilibrium.

Conclusions

It is postulated that:

1. The blood and vascular alterations of normal pregnancy are due to the presence of two factors at the placental site: (a) a modified arteriovenous fistula; (b) an area of resistance growing within the shunt.

2. The blood and vascular alterations of pre-eclampsia-eclampsia are an abnormal accentuation of those found in normal pregnancy due to an increased resistance at the placental site.

3. The increased resistance is not necessarily dependent upon the number and/or size of the chorionic villi, but rather upon the extent of effective blockage to the flow of maternal blood across the placental site.

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CONGENITAL HYDROMETROCOLPOS: REVIEW OF THE LITERATURE AND REPORT OF A CASE WITH UTERUS DUPLEX AND INCOMPLETELY SEPTATE VAGINA

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HYDROMETROCOLPOS is a congenital anomaly occurring usually in infancy and early childhood, associated with obstruction of the vaginal outlet, with varying degrees of cystic dilatation of the vagina and uterus by retained, nonsanguineous secretions. In a search of the literature references to thirty-one acceptable cases have been found since that of Godefoy[1] in 1856. This is in interesting contrast to the much larger number of reported cases of hematocolpos, in which the vaginal obstruction with retained menstrual blood becomes manifest after puberty. We are not concerned with the latter group at this time.

Some of the papers in the older European literature have not been available for study but reference to them is to be found in other publications. They are included here for the sake of completeness.

Budin[2] reported the case of a newborn infant who apparently recovered following incision and drainage of milky fluid. He mentioned that he had seen a second case in Florence in 1881, but does not describe it further.

Commandeur[3] in 1904 reported one case, that of an infant of 8 days, in whom incision and drainage yielded 100 c.c. of milky fluid. He mentioned by name nine other reports which he found up to that time (Godefoy,[1] Breisky,[4] Gervis, Bryck, Veit, Stroetter, Vitrac, Budin,[2] Barnes) but gave no further references to these papers.

Cranwell[5] in 1905 described the case of a 1-month-old infant with retention of vaginal fluid, urine, and feces. The thin membrane which occluded the vagina was incised and fluid under pressure was released. The child died, and at autopsy the membrane was found to be 1 mm. in thickness and was located above the perforate hymen.

Spencer's[6] case was that of an 11-week-old infant in whom incision into a bulging mass in the vagina yielded 1 dram of fluid. Another case was reported by Bjerrum.[7]

In Bonnet's[8] case the hymen was centrally perforate, with a blind pocket above it, due to an imperforate vagina.

Kereszturi[9] reviewed the literature in 1940 and recorded seven cases (Melodia,[10] Guilleminet and Gayet,[11] Breisky,[4] Bunzel,[12] Rocher and Balard,[13] Salazar de Sousa,[25] and Godefoy[1]) which she found in the Continental European literature extending back to that of Godefoy in 1856. Two of these seven cases (Godefoy[1] and Breisky[4]) were mentioned by Commandeur. Of these seven cases, two of the children were of ages 6 and 11 years, respectively, and five

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were under 2 months of age. Kereszturi's case was that of an 8-week-old infant, in whom an imperforate hymen led to hydrocolpos in early infancy, with the development of hydroureter and hydronephrosis, followed by pyuria and bacilluria. The patient recovered following drainage of about two ounces of "milky fluid." An intravenous urogram was found to be normal at the age of 22 months.

Three additional cases were reported in 1940 by Mahoney and Chamberlain.[14] The first of their patients was 2 days old when an abdominal mass was found to extend above the umbilicus. The protruding septum in the vagina was incised and the child made an uneventful recovery. The second case was that of an infant of 3 weeks, found to have a lower abdominal tumor with associated anuria and numerous watery stools. This child also made an uneventful recovery following incision of the vaginal septum. Their third case was that of an infant 1 day of age, having an imperforate anus, atresia of the esophagus, and a tracheoesophageal fistula, which resulted in aspiration pneumonia, of which the infant died.

In 1941, Bowen[15] reported the case of a 12-year-old girl, one of identical twins, whose sister had a perforate hymen. The patient complained of lower abdominal discomfort and a mass was found extending from the pelvis to the umbilicus. The bulging of the hymen was more prominent upon straining. Incision yielded "about two quarts of milky white fluid." The discharge subsided gradually over a two months' period, and menstruation began about five months after the incision, approximately five months after menarche in the normal twin.

Rosenblatt and Woolley[16] in 1943 reported the case of a 17-day-old infant with urinary retention in whom the diagnosis of cystic vagina was made by injection of an x-ray opaque medium. An incision at the point of vaginal atresia led to drainage of the fluid with recovery by the patient.

Morris[17] again reviewed the literature in 1945 and reported a case of a 7-week-old infant with swelling of the feet, cyanosis of the lower extremities, and urinary retention due to pressure on the pelvic vessels and displacement of the bladder by a large cystic mass involving the vagina and uterus. This child was subjected to laparotomy and collapse of the mass, but developed a fecal fistula and died 34 days postoperatively. Morris mentioned 2 other cases from the German literature, not mentioned in Kereszturi's review. One of these, by Althoff,[18] reported in 1941, was the case of a 14-year-old girl who complained of backache of six weeks' duration and was found to have a large abdominal mass. Fifty c.c. of cloudy serous fluid was withdrawn by puncture of an "imperforate hymen," but a larger mass remained and 2,200 c.c. of similar fluid was obtained by puncture of this mass, following laparotomy. The patient recovered but remained amenorrheic after the operation. The case described by Markus[19] was that of a 72-year-old woman with vaginal stenosis and hydrometrocolpos. The etiology of the stenosis was not definite, but senile vaginitis was advanced as a probable cause by the author. This case should perhaps not be considered in the present group, but it serves to illustrate the possibilities of vaginal cyst formation. McSweeney[20] reported in 1946 the case of a 40-year-old white woman, with a watery, purulent vaginal discharge for two years. She had menstruated normally with menarche at 13 and with periods of 8 days at 28 day intervals. Periods ceased at the age of 39. Three weeks before examination she developed a foul discharge and was found to have a "congenital" anomaly of the vagina with the lower segment about one inch in length. No sinus could be demonstrated between the lower and upper segments. Because of the purulent nature of the discharge and the presence of a larger mass above the vaginal septum, a hysterectomy was done and the base of the upper cyst was found to be adherent to a dense fibrous septum at the upper pole of the lower

segment of the vagina. This finding was considered by the author to be further evidence of the dual origin of the vagina from the müllerian system and the urogenital sinus.

Schell[21] reported in 1948 the case of an infant found to have urinary retention soon after birth. The mass extended 2 cm. above the umbilicus and the cyst protruded between the labia. The extent of this cyst was demonstrated by roentgenogram following the injection of Diodrast. Four hundred c.c. of mucoid material were drained following incision of the cyst wall. Seven months later the uterus was still enlarged but had decreased in size.

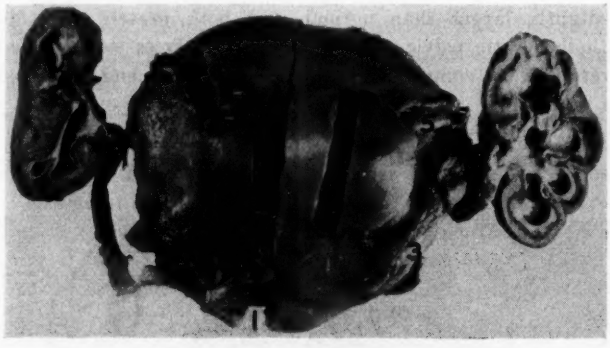

Fig. 1.—Gross photograph of the specimen viewed from above: (*1*) bladder, (*2*) posterior wall of the cystic vagina, (*3*) ureter, (*4*) left uterine cornu, (*5*) Fallopian tube, (*6*) ovary (one-half normal size).

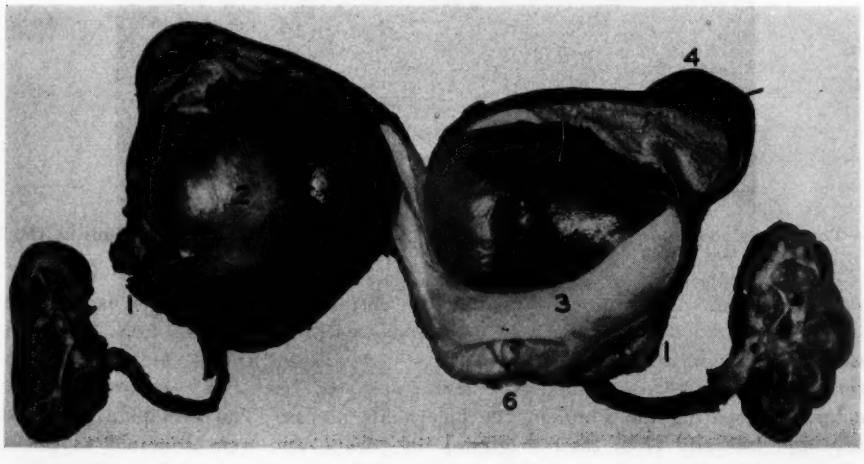

Fig. 2.—The specimen opened sagittally to show: (*1*) the compressed bladder, (*2*) the smooth lining of the vaginal cyst, (*3*) the partial vaginal septum, and (*6*) the constriction at the vaginal outlet. The wrinkled mucosa of the endocervix and right uterine cornu is shown at *5* and a probe extends through the left cervical canal. The dilatation of the ureters and renal pelves is evident.

Another case (age 2½ years) was mentioned by Curtis[22] in the fourth edition of his *Textbook of Gynecology*. This case apparently had not been reported otherwise.

In none of these reports has there been any other anomaly of the genitourinary system. In the case to be described there was a coexistent uterus duplex with incompletely separate vagina in a newborn infant.

History.—The infant was born at term by normal delivery. The mother was a primigravida who had had a normal and uneventful prenatal course. At birth, the child was cyanotic and on examination was found to have a large, soft tumor mass which completely filled the pelvis and lower abdomen. The infant failed to breathe, and efforts at respiratory stimulation were unsuccessful. She was pronounced dead 10 minutes after birth.

At autopsy the body weighed approximately five pounds (2,250 grams). The abdomen was distended by a palpable mass, extending slightly above the level of the umbilicus. The external genitals were normal for a newborn female, without bulging of the mass into the vagina. No other abnormalities were noted on external examination. There were no anomalies found in the heart. Both lungs were atelectatic, and the diaphragm was elevated. The abdominal organs were displaced by the presence of the mass protruding from the pelvis. The kidneys were slightly larger than normal, and both ureters were dilated above their point of contact with the cystic pelvic mass. The renal calyces were dilated, and the cortices were thin. The ureters were compressed between the mass and the posterior and lateral walls of the pelvis, and from the point of contact with the cyst they were smaller and fused with the cyst wall but could be separated by dissection. They could be traced around the surface of the cyst into the small compressed bladder situated on its anterior-inferior

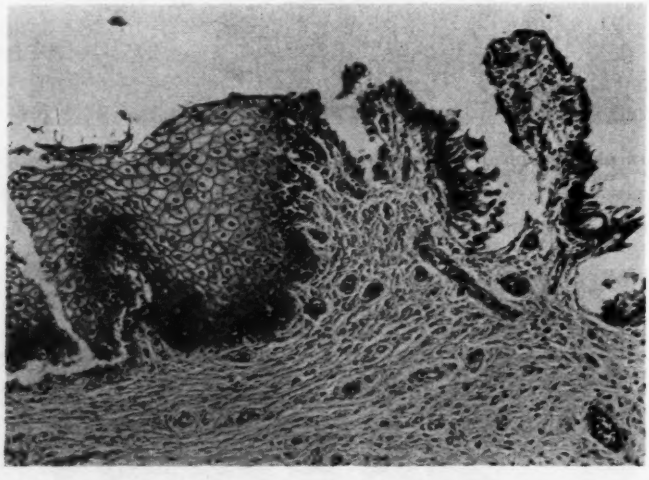

Fig. 3.—The squamocolumnar junction of the vaginal and endocervical epithelium at the border of the wrinkled disc in the dome of the vaginal cyst. (×435.)

surface. The rectum was compressed against the posterior wall of the pelvis, but there appeared to be no obstruction, inasmuch as meconium was present at the anus. After removal and closer examination, this cystic mass measured 8 by 7 cm. On the anterosuperior surface there were two connected, domelike cystic structures, each measuring approximately 1.5 cm. in diameter, representing the fundi of the bicornuate uterus. The Fallopian tubes extended posteriorly and laterally from their origin in the cornua and were adherent to the wall of the larger cyst. The round ligaments extended anteriorly and inferiorly. The ovaries were located near the fimbriated extremities of the Fallopian tubes and were of approximately normal size for an infant of this age. On opening the mass by a sagittal incision it was found that the larger vaginal cyst and the distended uterine cornua were filled with mucoid material, slightly yellowish in color. The wall of the vaginal cavity measured approximately 3 mm. in thickness, and its lining was smooth, with numerous small veins visible beneath the mucosal surface. There was an incomplete semilunar septum located along the anterior inferior surface of the cyst inserting superiorly at the border of a roughened, wrinkled disc of endocervical mucosa in the dome of this cyst. The hiatus in this septum measured 4 to 5 cm. in diameter. The two cystic uterine cornua located on the dome of the larger cyst were found to be lined by ragged, irregularly folded mucosa. The orifices of the

Fallopian tubes were represented by small depressions around which the mucosa was arranged in a radial pattern. A small probe could not be inserted into these orifices, but the tubes were patent from the fimbriated extremities to the cornua, at which point they made a sharp downward turn to pass into the uterine wall. There was apparent tubal obstruction at the endometrial surface. The myometrium measured 3 to 4 mm. in thickness. The zone of the everted endocervical mucosa was approximately 3 cm. in diameter with two foramina, each leading into one of the uterine cavities. These foramina measured from 2 to 4 mm. in diameter. The bladder was located upon the anterior inferior surface of the vaginal cyst and was compressed to a volume of less than 5 c.c. The base of the vagina was occluded by what appeared to be a constricted, but probe-patent channel lined by longitudinally wrinkled mucosa. There was no bulging between the labia on pressure over the mass prior to its removal from the body. Some thickening or fibrosis was evident at this point of constriction, but its inner orifice in the cyst was partly covered by the vaginal septum which could exert a valvelike effect in the intact structure.

Microscopically, the vaginal cyst was lined by flattened keratinized squamous epithelium from 2 to 8 cells in thickness, overlying a thin fibromuscular wall. The cornua of the uterus were lined by cuboidal to low columnar epithelium which covered many small palillary processes, having a loose but cellular stroma, of large distinct decidua-like cells. The crests of most of these papillae were infiltrated by polymorphonuclear neutrophilic and eosinophilic leukocytes with a few lymphocytes. On the surface of the endometrium, keratin debris and desquamated epithelial cells were present. The endocervical mucosa forming the disclike area in the dome of the vaginal cyst was of the same structure as that lining the uterine cavity. A slight increase in fibrous tissue was found in the wall of the vagina at its point of constriction. Sections of the interstitial portions of the Fallopian tubes were lined by cuboidal epithelium.

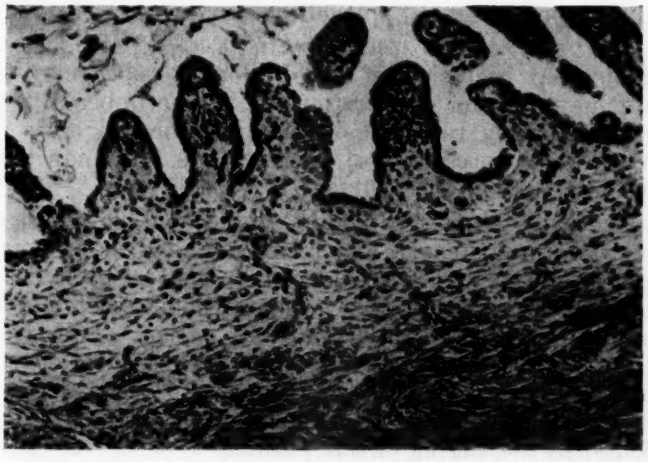

Fig. 4.—The uterine wall, to show the papillary endometrium from the fundus of the uterus, with the decidual reaction. Note cellular debris in the upper left corner of the photograph. (×435.)

Comment

The facts thus far available indicate that at least two factors contribute to the development of hydrocolpos in infancy. The first of these is obstruction which exists in the lower vagina, and which is apparently due to failure of fusion of the superior and inferior vaginal segments, rather than to an imperforate hymen. Koff[23] has brought out this point in his studies of the embryology of the vagina. Using wax-plate reconstructions and millimeter plates of approximately one hundred twenty-five female embryos, he concluded that the

upper part of the vagina develops from the Müllerian ducts, but that these structures play no part in the development of the lower one-third of the vagina, which is formed from an invagination of the urogenital sinus, while the hymen is formed from evaginations in the posterior wall of the urogenital sinus. The finding of a thick fibrous membrane occluding the vagina above the level of the hymen in the reported cases lends support to Koff's view, and the constriction in our case suggests that the union of the upper and lower segments of the vagina was incomplete. The hymen itself is usually a thin structure and is probably not involved primarily in the type of retention under discussion. Support is given Koff's views by those cases which are adequately described.

The second factor is that of hypersecretion above the point of obstruction. Evidence that this secretion does not occur in all cases in which there is obstruction is presented by the occurrence of hematocolpos after puberty. It would seem from the comparatively large number of reported cases of hematocolpos that vaginal and uterine secretion is depressed in these patients until the onset of menstruation, or that only those patients having abnormal uterine secretions during infancy can develop an enlarged and cystic vagina and uterus. The factors which influence this activity are not understood. Dobszay[24] has shown that the physiological vaginal secretion can be induced in infants by adequate estrogen administration provided the flora of the vagina is of the adult type. This cannot apply directly to the cases in question because of the vaginal obstruction and lack of opportunity in developing an "adult vaginal flora."

Endocrine secretions in the mother can pass transplacentally to the fetus, as has been shown also by Dobszay, and observed often in newborn infants, so that endocrine-induced functions may develop directly in the fetal tissues. The finding of a decidual reaction in the infantile uterus, and the common occurrence of an adult type of vaginal epithelium during early infancy bear out this fact.

It is possible that occlusion of the Fallopian tubes may play a part in vaginal and uterine retention of secretions in the prepubertal period, but there is, so far, no investigation reported of tubal patency in cases of hydrometrocolpos, other than in the present case in which the Fallopian tubes were found to be occluded at the endometrial surface.

Of the cases reviewed, one probably should not be accepted in this category of congenital vaginal stenosis and is not included in the total of acceptable cases. That of Markus in a 72-year-old woman was attributed by him to senile vaginitis. This obstruction, whatever its cause, should be classified more properly as a secondary stenosis. The 40-year-old patient of McSweeny had menstruated until the age of 39, when the vaginal occlusion developed. This should perhaps be looked upon as one of the late complications of a congenital constriction but not occlusion of the vagina, and was probably similar in nature to the lesion found in the vagina of our patient.

The method of treatment has consisted of incision of the obstructing septum with drainage of the retained fluid. The cyst can sometimes be demonstrated by injection of radiopaque material through the vaginal septum to outline the lower abdominal mass in instances of questionable diagnosis. The immediate danger to life in infants lies, not in the cyst itself, but in the ureteral and rectal obstruction which has been demonstrated in reported cases. When the anomaly is borne in mind, its diagnosis should not be difficult and it should constitute one of the more easily relieved abdominal masses in infancy, not usually requiring laparotomy. Other associated anomalies should be searched for, though in only two instances have they been noted: the tracheoesophageal fistula and imperforate anus of one of the cases of Mahoney and Chamberlain, and the uterus duplex and partially septate vagina of the present authors.

Summary

The case of a newborn infant with hydrometrocolpos involving a uterus duplex and septate vagina is reported. The cystic vagina compressed and obstructed the ureters, with resulting hydroureter and hydronephrosis.

Of the thirty-one cases of congenital hydrometrocolpos in the literature, seventeen patients were known to be under the age of 2 months, one was aged 2½ years, two were 6 and 7 years, respectively, and three were over 12 years of age. The reports of eight of the cases, in the older European literature, were not available for study.

It is evident that the cystic dilatation of the vagina and uterus can be demonstrated by the injection of radiopaque media, and the obstruction relieved by incision of the imperforate vaginal septum, usually with recovery in cases which are not complicated by prolonged urinary obstruction or infection.

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DEPRESSIVE REACTIONS DURING GESTATION AND THE PUERPERIUM

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PREGNANCY and childbirth frequently catalyze depressive reactions of varying intensity in especially predisposed women. This proclivity is apparently related to a particular kind of early life situation which increases psychologic vulnerability.

Organic Factors Play Limited Role

Pathophysiologic changes germane to gestation and the puerperal period may have a direct bearing on these emotional reactions. I refer to: (1) hormonal changes and imbalances, (2) elaboration of toxic products, (3) nutritional disturbances, and (4) physical exhaustion resulting from pregnancy, parturition, and lactation.

It is my belief that such organic factors do not act as specific causal agents in depressive reactions, but act rather to lower the threshold of resistance to psychic injury which the advent of the child represents.

There are, to be sure, psychoses related to clearly definable toxic-exhaustive factors of gestation; but in these the clinical picture is not depression but a rapidly occurring, delirious, confusional state, which responds quickly to an eliminative-supportive regime.

Some question exists as to the influence of hereditary factors on depressive reactions. It is difficult to disengage the influences of heredity and environment. However, as I shall demonstrate in this paper, environmental influences in early life appear sufficient in themselves to account for the breakdown of adequate behavior patterns at this important milestone in woman's life.

Early Family Background All Important

Romm[1] has advanced the hypothesis that every person unconsciously wants to be an only child. Certainly, behavioral evidence in support of this tenet is clearly observable in infancy and childhood. During the usual vicissitudes of physical and psychological growth and development, this primitive pattern is modified and tempered, and its remnants are satisfied through constructively ambitious strivings and worthy achievements.

Ordinarily, character maturation has progressed enough by the time of marriage and pregnancy to enable women to handle the ordinary problems of rivalry and competitiveness in an adequate manner. There are, however, particular kinds of life situations which tend to fix and consolidate the infantile need to occupy the center of the stage—to be an only child—and which permit this need to persist in a relatively pristine form, albeit disguised by the façades of chronologic growth.

The following series of case reports of women showing depressive reactions in childbirth are introduced to high light and clarify a particular psychogenic relationship between past life situation and precipitating event which has special implication in treatment. Cases 1 and 2 concern women who were in fact only children. In Cases 3 and 4, on the other hand, the effect of the family situation was to rob the patient of the usual period of dependent childhood and to hold in abeyance and thus intensify the need for protection and exclusive love and attention that are the share of the only child. The case material presented, therefore, shows the early background of each patient to be essentially that of an only child, either in actuality or psychologically.

CASE 1.—Mrs. H. R., aged 24 years, was brought to the sanitarium because of a severe, retarded depression. She had become progressively more depressed and retarded since the birth of a son four weeks previously and, upon admission, was in a state of near muteness.

During gestation and the puerperium, both the patient and her husband had eagerly awaited the birth of the child; especially so, as three previous pregnancies in four years of marriage had terminated in miscarriage. (Medical and gynecologic examination had disclosed no cause for repeated miscarriage.)

During the last, successful pregnancy, the patient was constantly preoccupied with thoughts of possible miscarriage. The husband, aged 35, states: "I had to be like a mother to her all during the pregnancy. I looked after every need and reassured her constantly." The patient often spoke longingly of wanting to be with her mother who lived in another city. In general she felt well during most of the pregnancy, although she had a frivolous appetite, desiring unusual foods, often in unusually large quantities.

Signs of moodiness and withdrawal were intensified in the last trimester and, after delivery, her mental condition deteriorated rapidly to the picture presented upon her admission to the sanitarium.

Early history: The patient, an only child, was born when her mother was 20 and her father 45 years of age. She was close to both parents, especially to her very devoted mother. The father is described as a very kind and gentle old man, almost motherly in nature.

The mother and father were divorced when the patient was 8 years old—a great blow to the child, who was much attached to her father—and the mother devoted herself completely to her daughter. Emotional ties between mother and daughter were pathologically tight until, just after the patient's 13th birthday, the mother remarried. In a violently jealous reaction, the patient refused to attend her mother's wedding; and, to date, she remains on poor terms with her stepfather.

At the age of 20, Mrs. H. R. married a man substantially older than herself, who is very protective of her. The marriage is quite happy, and, in spite of her disappointment over the miscarriages, the patient was able to find some substitute satisfaction in preparing to be a nursery school teacher. The husband reports that the patient is jealous and overly sensitive of any attentions he pays to his parents or, indeed, to anyone else.

Comment.—This patient was in actuality an only child, with an early life situation that strongly reinforced the "only child" complex. She clung tenaciously to all of her sources of emotional supply, and her reactions clearly indicated a need for exclusive control over them. She reacted neurotically over the "intrusion" of a stepfather; later, over her in-laws; and, now, over the intrusion of her own child, unconsciously visualized as a rival. The three miscarriages seem to have had a psychogenic basis, and they represented a way of eliminating potential rivals.

CASE 2.—Mrs. O. P., aged 25 years, of better than average intelligence, entered the sanitarium three months after the birth of her first child, a daughter. The patient ap-

peared obviously depressed and mildly retarded and complained of insomnia and anorexia, symptoms which had remained entirely unresponsive to medical management—sedatives, stimulants, hormones, vitamins and the like.

During gestation and the puerperium, although she had apparently welcomed the pregnancy, the patient had been troubled sporadically by feelings of impending catastrophe; and though there were never any physical indications of miscarriage, she lived in constant apprehension that she would miscarry or that the baby would be born dead or deformed.

The patient felt unusually happy after delivery and for the short period of hospital confinement. She enjoyed the visits of members of her family and, particularly, those of her husband. At the same time, she experienced a growing apprehension about her ability to care for the baby, for she wanted to do a "perfect job" and she feared her performance might be less than perfect.

After her return home, she felt profoundly depressed and unequal to the task of caring for the baby. She showed aversion for nursing the baby, complained that she could not stand the baby's mouth on her breast. She became progressively more depressed and retarded, and attempted to compensate for her lack of interest in the baby by a pseudomotherliness, an excessive concern over the baby, demonstrated in worry about feedings and the frequency with which diapers should be changed. The baby's cries and grimaces terrified her to the point where she was completely immobilized.

Shortly before she came to the sanitarium, the patient noted that her body felt completely numb when she would lie in bed at night; accompanying this feeling was the severe apprehension that her husband would expect to have intercourse and that she might become pregnant again. She came to the sanitarium willingly and requested that she have private nurses.

Early history: Mrs. O. P., the younger of two sisters, was adopted by her maternal aunt and uncle when she was two years old, shortly after the death of her mother. As her father returned at that time to the country of his birth with the older sister, the patient has not seen either her father or sister since her second birhday. The patient was raised as an only child by excessively protective and apprehensive foster parents; and she remembers frequent threats that if she misbehaved, she would be "given back" to her own father and paternal grandmother, with whom her father now made his home. These threats always upset her greatly.

Comment.—This patient, raised as an only child by devoted parent surrogates who lavished attention upon her, had a chronic dread that she might lose the love of her foster parents and be forced to share with her sister the meager attention she might receive in the home of her paternal grandmother. She developed into a neurotically compliant person so that this "catastrophe" would be avoided. However, with the birth of her own child, the very situation which she had assiduously worked to avoid was, for her, now a reality. A rival was on the scene, and she would now have to share her husband's love and attention with their child.

The body numbness is an interesting representation of the overdetermination of neurotic symptoms. It is at once (a) a defense against the musculoskeletal manifestations of hostility, (b) a defense against the investment of tenderness in the child, and (c) a protection against another pregnancy, since not only is intercourse unlikely in this condition but a "numb" or "dead" body is incapable of reproducing itself.

CASE 3.—Mrs. M. H., aged 28 years, entered the sanitarium six weeks after the birth of her second child—a son this time—in a state of agitated depression. She had no appetite and had lost a great deal of weight.

She remarked: "I keep thinking I will kill my baby, and it's driving me crazy." "I'm afraid I'm losing my mind." "Do you suppose I really don't care for my child? I can't seem to believe that."

The patient had cried hysterically a great deal since the birth of her child. Her crying and wringing of hands were of a very dramatic nature, making it necessary for her husband to quit his job and remain constantly at her side.

At the first consultation the patient was advised to enter the sanitarium but she refused, preferring to remain at home with her husband in attendance.

One week later the patient was seen again. The picture of hysterical crying, marked agitation, insomnia, anorexia, and intense feelings of unworthiness had become worse. She constantly monopolized her husband's attention by her dejection and by lamenting and questioning: "Am I losing my mind?" "Is this really happening to me?" "Will I kill my baby?" "I'm afraid I'll never get well." "I don't deserve forgiveness."

The patient had reacted with mild but transient depressive reaction after her first delivery. She had gone through her first period of gestation without apparent physical or psychic complications, although she had not desired either pregnancy and consented to the second one with great reluctance.

The husband indicated that he was very attentive to his wife during her pregnancies, catering to her every whim. He believed that his wife was jealous of his attentions to their first child, of whom he was extremely fond.

The second pregnancy was complicated from the very beginning by frequent vomiting; and toward the middle of the pregnancy interruption was considered because of weight loss and general debility. Although the pregnancy was carried to a successful termination, the patient's condition made it impossible for her to nurse or otherwise care for the child. In fact, she needed more care than the infant, and her behavior patterns were of such nature as to demand the constant attention of everyone in the household. The patient's mother cared for the child.

Early history: Both of this patient's parents are described as neurotic, inadequate persons. The father, a gentle, passive individual with no trade or profession, who supported his family with difficulty, died of cardiovascular disease in his middle fifties. Our patient is the third of four children; the others were boys. Although all of the youngsters were close together in age, they all turned to M. H. for help and advice; and she has always felt that she was forced to grow up too fast, because of the dependence of the others on her. The patient drew comfort during this period from commiserating conversations with her hard-working and long-suffering mother.

Mrs. M. H. was married at 23 to a man who might be said to be masochistically devoted to her and the children. His behavior toward her is that of a doting and busy mother.

Comment.—The patient's infantile need to occupy the center of the stage—to be the only child—was constantly thwarted, and her own dependent cravings within the family constellation remained unfulfilled. In a sense, she was able to find a partial satisfaction as the only good and competent child. She gave a mother's care to the other children; by this unconscious psychologic maneuver, she managed to remove the other children from her mother's solicitude and occupied the place of only child—the only child who had need of her mother's personal care and attention. Although this maneuver apparently was successful and, outwardly, the patient managed adequately, the reservoir of unfilled, dependent needs rose ever higher.

Additionally, the patient found some special fulfillment as the youngest child until the birth of her youngest brother, toward whom she shows exaggerated feelings of rivalry and disdain.

Some satisfaction was found in marriage, in her relationship to a motherly husband who showered her with affection. She strove desperately to be the recipient of *all* her husband's affection, to be the only one. She was able to cope with the arrival and management of her little daughter; but it appears now more than coincidental that the birth of a son, perhaps unconsciously reminiscent of the abhored brothers, and particularly of the youngest brother, who usurped the position of youngest child, should precipitate the acute depressive reaction.

CASE 4.—Mrs. A. S., aged 36 years, complained of severe depression, prolonged crying spells, suicidal thoughts, and fears that her premature baby might not live, having got off to such a bad start. She was plagued with ideas like: "I'm not sure I did the right

thing to have a baby at this time. I feel that perhaps I will not be able to care for him properly.'' ''Maybe it would be better if someone adopted the baby before we have a chance to get too attached to him.'' She felt convinced that these thoughts were the result of physical difficulties. Mrs. A. S. felt very guilty over her own suicidal thoughts, because she knew the infant needed her attention.

When Mrs. A. S. was first seen in the fifth month of her pregnancy, she showed preoccupation with her ''peculiar appearance'' because of the abdominal enlargement. She tried to hide the fact of her pregnancy from others and even attempted to deny the fact to herself and sought for evidences of bleeding at the usual time for her menses. In the last trimester she actually did have vaginal bleeding, and her obstetrician was alarmed over the possibility of a placenta previa. She spent much of the third trimester in bed, with private nurses in attendance. During this period she felt reasonably well.

Her 47-year-old husband, a successful manufacturer ordinarily engrossed in his work, devoted much of his time and attention to her during this complication of her pregnancy. He was most eager to have an heir.

Parturition occurred prematurely, but the infant was viable and was cared for in an incubator. During the period of hospitalization, the patient appeared reasonably well; but, upon returning home with the baby, her feelings of depression suddenly increased.

Mrs. A. S. loved her husband and greatly enjoyed the material comforts he had provided in the three years of their marriage. Accordingly, she was puzzled that she should have any but the most loving and maternal thoughts toward this child which her husband wanted so much.

Early history: Mrs. A. S., the oldest of four children, was born in a small farming community to impoverished parents with rigid and narrow moral standards. Her brother and two sisters were substantially younger than the patient; and, quite early, she was given a great deal of responsibility in the household. As her parents, spoken of as good and kindly people, were too busy with the problems of daily survival to devote much time to their children, the patient served as ''assistant mother.'' She accepted the task of caring for the other youngsters in good spirit; but when, at times, her responsibilities became too much for her, she engaged in flights of fancy in which she was the only, pampered child (a condition which obtained in her marriage until the arrival of her baby). At the age of 18, Mrs. A. S. left home and studied to be a schoolteacher. Up to the time of her marriage, she taught the lower grades in elementary school; and, although she was not an inspired teacher, she was a competent one. At the close of the school day, she was able to shut her mind to the problems of her little charges until the following day. Many childhood fantasies were actually fulfilled in her marriage; and because she appreciated her husband's ability as a provider, the patient was able to tolerate his absorption in his work. She wished, however, that her husband had the capacity to close the door on his work when he left for home, as she had done when she taught school.

Her first significant emotional disturbance came with her pregnancy, and to her the feeling was quite unfathomable.

Comment.—Through the accident of her early life circumstances, this patient could not find fulfillment of the need to be an only child. In fact, she had little opportunity to be even a child among other siblings. She found the complete realization of her need to receive a loved one's full attention, ultimately, in a late marriage. The fulfillment, unconsciously postponed for so long a time, could not be compromised. The infant was an intruder, an interloper who could only detract from her newly found happiness. Her reactions were strong, and it was evident that she wanted to hide, even from herself, the fact of her pregnancy.

Quite apart from the need for exclusive care and affection, another important unconscious psychologic factor undoubtedly entered into this patient's reaction toward her child. As a youngster, her parents had warned her, grimly, that pregnancy is the supreme punishment for sin and sexual congress. Now, her pregnancy furnished evidence to all eyes of indulgence in the ''forbidden pleasures'' of sex. This attitude, carried over into the marriage relationship, accounts in part for the patient's wish to hide the fact of her

pregnancy and for the excessive attention she paid to her "peculiar appearance" during pregnancy.

Comment

In general, the depressive reaction psychodynamically represents a despairing call for exclusive care and affection. The depression is catalyzed by a feeling of loss of the necessary emotional sustenance, and it is a method of coercion directed against the thwarting environment for more supplies. The depression also represents a self-punitive measure, required because of the guilt engendered by the destructive hatred of the disappointing objects.

These mechanisms are clearly evident in the patients discussed above. To begin with, all these women, because of special early life's circumstances, showed a persistence of the childhood need to be the only one to an inordinately large degree inappropriate for their chronologic ages. The emotional supplies they needed were very close to the infantile variety; adult, sublimated substitutes were insufficient. In each case examination of the marriage relationship disclosed that the husbands were unconsciously looked upon as mother images—sources of supply. The patients were happiest when their husbands provided additional undisguised, motherlike care.

Depressive symptoms tended to become less severe with an increase in the husband's overt concern and physical presence. Similarly, the depression decreased with increased nursing care and special attentions.

Contrariwise, with greater attention paid to the baby—such as occurred when the confinement period was over and mother and baby returned home—the depression became more profound. The discovery that the world is more interested in and concerned with the baby than with its mother was most unacceptable. Hostility toward the baby was obvious in many ways, not the least of which was the inability to nurse the child. Anger toward the husband was evident in the peevishness demonstrated—plaintiveness, demandingness, denial of sex gratification, and, in general, depriving the husband of freedom to do anything but remain in constant attendance. Basically, however, at a deeper, unconscious level, anger is directed at the patient's own mother. The patient visualizes her child not as her own offspring but rather as a sibling rival.

The excessive need for exclusive care and attention which characterizes women who respond with depressive reactions to gestation and the puerperium is only one factor in the breakdown of adequate behavior patterns, albeit a nuclear one. Another factor that I have touched upon briefly in this paper is the feeling that pregnancy is visible evidence of indulgence in prohibited sexual activity. Other psychologic factors also undoubtedly contribute to depressive reactions.

Implications for Treatment

The patient's basic ability to tolerate rivals and her need for a monopoly of maternal love are factors which can be affected significantly only within a psychotherapeutic situation which will permit and encourage healthy character maturation. The whole area of jealousy, rivalry, and competitiveness, the need to receive and the difficulty in giving and sharing, the unconscious ways of fulfilling neurotic demands—these must be worked through appropriately.

If beginning signs of emotional imbalance are observed and psychotherapy is begun early in pregnancy, severe psychopathologic reactions may be avoided. It is the responsibility of the obstetrician to be on the alert for such early signs, and to see that the patient secures necessary psychiatric treatment.

The re-establishment of physiologic equilibrium may be aided by certain auxiliary measures; I have in mind hormonal therapy and nutritional aids.

Recognition that pathophysiologic factors are not basic causes of depressive reactions makes it possible to utilize these measurees in their proper ancillary role.

At times, in severe depressions, the obstetrician may wonder whether therapeutic abortion would not be wise. It might seem that elimination of the rival would better the situation. This is not necessarily the case for the guilt and self-reproach resulting may serve only to intensify the depression.

In many cases, especially the milder ones, psychotherapy alone may be sufficient. In others electroconvulsive therapy may be necessary.

Electroconvulsive therapy produces its most satisfactory results in depressive reactions. It is often a matter of expediency to apply electroconvulsive therapy without delay in cases where a strong suicidal trend or intense agitation is present or, indeed, in the treatment of any depressed patient in whom the symptomatic picture prevents the establishment of an effective psychotherapeutic relationship. Shock therapy, used in this way, may prevent a long siege of tube feedings and shorten the period of hospitalization. However, electroconvulsive therapy should not be employed routinely in all cases as soon as the diagnosis of depressive reaction is made. (Patients in Cases 2 and 4 recovered without electrical treatment.)

The improvement resulting from electroconvulsive therapy is probably connected with (a) the draining off of some anxiety through the intense physical exertion, and (b) the allaying of guilt through a feeling of being punished. At all events, the exact way that electroconvulsive therapy effects changes in the symptomatic picture remains obscure. It does seem apparent, however, that electrotherapy cannot change the patient's basic ability to tolerate rivals or modify her need for a monopoly of her mother's love. Electroconvulsive therapy, though it produces symptomatic improvement, can only obscure these problems further if treatment ceases after the patient is brought back to her former level of adjustment. The homeostatic balance at this level is at best precarious and must depend upon accidental environmental beneficences and perhaps the mate's complementary neurosis to maintain itself.

If electroconvulsive therapy is used, it should be employed only to the point where an effective psychotherapeutic relationship can be established. It is not enough that the patient receive relief from currently immobilizing symptoms. The patient must be aided, through utilizable insight and emotional growth, to find fulfillment in an adult way in her role as wife and mother.

Because one of the fundamental sources of neuroticism is parental rejection of the child, it is important from the mental hygiene aspect that depressions of gestation and the puerperium be handled in this manner.

Summary

Four condensed case histories of depressive reactions during and following gestation are presented. The psychodynamics of this reaction type are discussed in terms of the thwarting of the patient's need to be the only child and her unconscious reaction toward her own offspring as if he or she were a sibling rival. Treatment implications are discussed, covering both electroconvulsive therapy and psychotherapy.

Reference

1. Romm, M. E.: Unpublished paper read at a joint meeting of the San Francisco and Los Angeles Psychoanalytic Societies, November, 1951.

5227 Santa Monica Boulevard

THE INCIDENCE OF MALIGNANCY IN THECA-CELL TUMORS

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IN 1932, Loeffler and Priesel[1] segregated six cases from a group of fibromatous ovarian tumors and designated them as "fibroma theca cellulari xanthomatodes." These were differentiated on the basis of histological and biological characteristics. Since these tumors simulated fibromas, many investigators were prompted to review their ovarian fibromas. This resulted in a rapid accumulation of cases and the establishment of the theca-cell tumor of the ovary as a clinical and pathological entity. By 1944, in a review of the literature by McGoldrick and Lapp,[2] 82 such tumors had been reported, to which the authors added three cases of their own. In recent years, substantial additions have been made[3-8] so that at the present time the number of reported cases exceeds 125.

To date, only five of these reported cases have been considered malignant by the authors. In three[11, 12, 15] metastatic lesions were present. The other two were considered malignant on the basis of their histological characteristics. We are able to report one more malignant thecoma with metastasis.

L. M., a 51-year-old white woman, para ii-0-ii-ii, was admitted to Kings County Hospital on Feb. 4, 1951, with a chief complaint of lower abdominal pain. She had had a similar episode on Dec. 11, 1950, which persisted for 24 hours. Her menses had begun at the age of 14 years, every 28 days, lasting 3 days. The last menstrual period had been Dec. 17, 1950. No menstrual abnormalities were present. She had had two normal full-term spontaneous deliveries and two spontaneous abortions requiring curettage. Blood pressure was 120/80, temperature 99.4° F., pulse 80, respiration 22. The abdomen was moderately obese. There was a freely movable, slightly tender, firm mass arising from the pelvis to within one fingerbreadth of the umbilicus. No tenderness, spasm, or evidence of fluid was present. Pelvic examination revealed a parous introitus with slight relaxation of the anterior and posterior vaginal walls. The cervix was posterior, firm and semi-fixed. There were a small erosion and a healed laceration present. No bleeding was evident. The uterine fundus felt nodular, hard, and was irregularly enlarged to the size of a 4 to 5 months' gestation. There was a pedunculated firm mass arising from the anterior wall. Clinical impression: fibromyomas of the uterus with degeneration.

Laboratory Findings.—The sedimentation rate was 24 in 60 minutes, white blood count 10,400, with 60 per cent polymorphonuclear leukocytes, the hemoglobin 15.5 Gm., urinalysis negative.

Operation.—Subtotal hysterectomy, bilateral salpingo-oophorectomy, and excision of a left broad ligament mass.

Operative Findings.—There was a small amount of free fluid present in the abdominal cavity. The right ovary was completely replaced by a solid tumor mass, measuring 14

by 8 cm., which was twisted on its pedicle. The left ovary, both tubes and the uterus appeared normal. In the left broad ligament, just above the uterine artery, a papillary, solid, friable, gray-white mass was noted.

The postoperative course was uneventful and the patient was discharged Feb. 20, 1951.

On March 2, 1951, the patient was started on a course of external radiation. A total of 3,000 r in air (200 kv., 0.5 mm. copper, 1 mm. aluminum filter, half value layer 0.9 mm. copper, skin target distance 50 cm.) to each of four pelvic ports was completed on May 22, 1951. At the time of her last follow-up examination, Jan. 30, 1952, the cervix was described as small, firm, and freely movable. There was no evidence of recurrence. Vaginal smear and cervical biopsy at this time were negative.

Fig. 1.

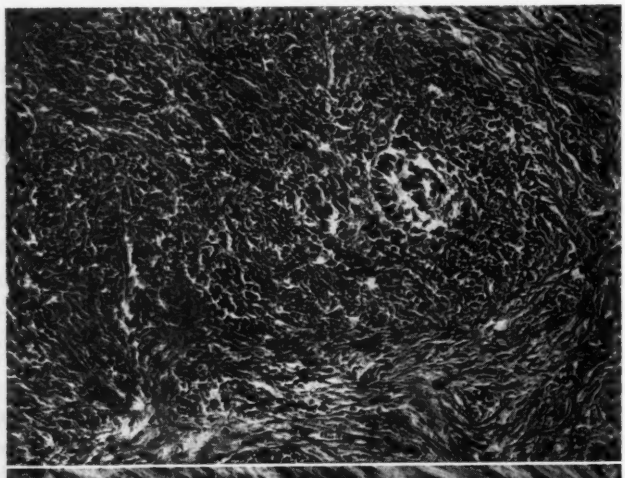

Fig. 2.

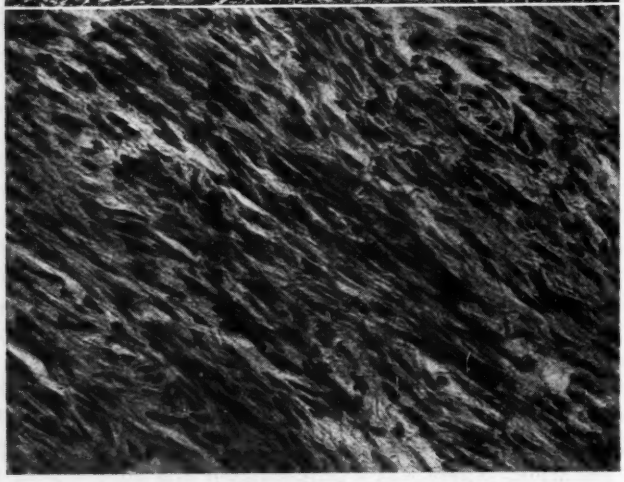

Fig. 1.—Section of thecoma showing rare granulosa-cell rest. (×200.)
Fig. 2.—Section showing broad spindle and epithelioid cells. (×350.)

Pathologic Anatomy

Gross.—The right ovarian tumor measured 15 by 8 by 7 cm. and had an irregular shape. The surface was firm, nodular, and tan except for a few small brown and blue discolorations. The tumor cut with increased resistance. The cut surface was predomi-

nantly tan but several areas had a yellow color. There appeared to be fibrous trabeculae coursing throughout. The uterus measured 5 by 4 by 6 cm. and was globular in shape. The myometrium was tan and had a homogeneous consistency. One fibromyoma measuring 0.5 cm. in diameter was present in the intramural portion. The left tube and ovary appeared normal, the latter measuring 3 by 2 by 1 cm. At one pole there was a serpiginous yellow area, approximately 1.5 cm. in diameter.

The tissue removed from the left broad ligament consisted of a single fragment measuring 2 by 1 by 0.5 cm. The tissue was gray in color and rubbery in consistency.

*Microscopic**.—Sections of the ovarian tumor, right, revealed densely packed, broad spindle cells, arranged in sheaths which interlaced in an irregular fashion. Some of the cells were epithelioid in appearance. Focal areas of hemorrhage and necrosis were present.

Fig. 3.

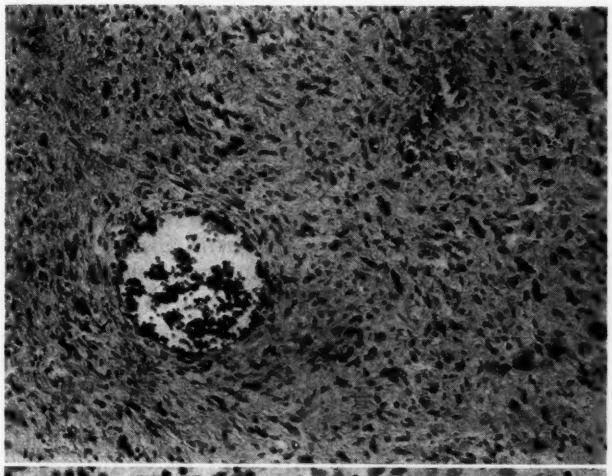

Fig. 4.

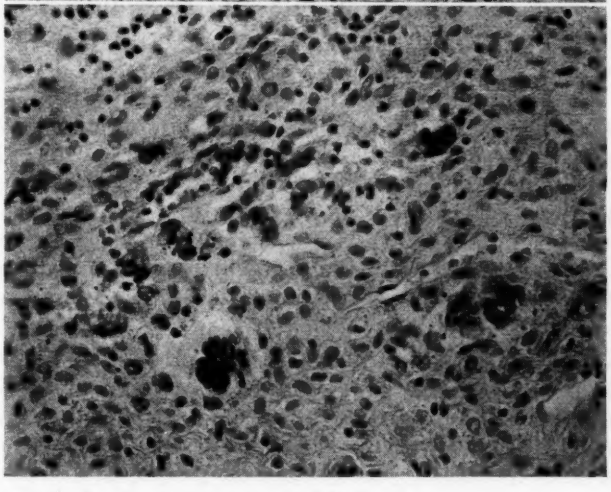

Fig. 3.—Section of metastatic lesion revealing alteration in cell structure. (×150.)
Fig. 4.—Higher-power view showing multinucleated cells. (×350.)

In two of eighty sections examined a few small collections of granulosa cells were noted (Figs. 1 and 2). Sections stained with Sudan IV revealed fine globules of intracellular fat. Corresponding areas revealed doubly refractile bodies present under the polaroscope.

*Grateful acknowledgment is made to Dr. Emil Novak for reviewing the material from this tumor.

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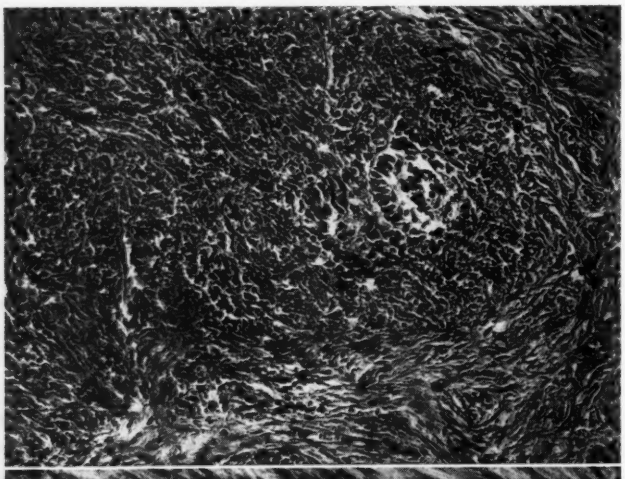
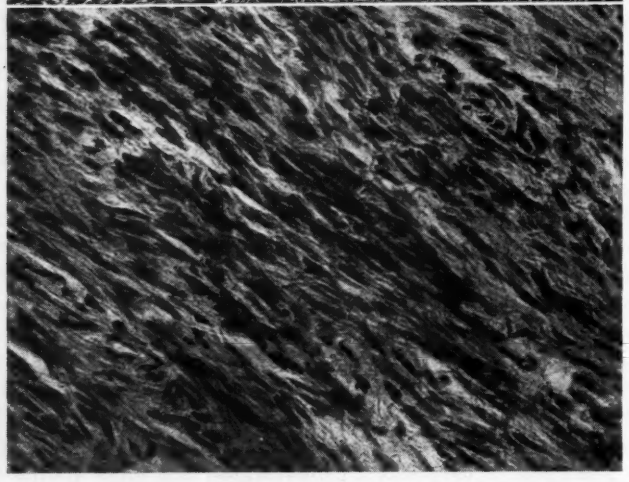


Fig. 2.



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The tissue removed from the left broad ligament consisted of a single fragment measuring 2 by 1 by 0.5 cm. The tissue was gray in color and rubbery in consistency.

*Microscopic**.—Sections of the ovarian tumor, right, revealed densely packed, broad spindle cells, arranged in sheaths which interlaced in an irregular fashion. Some of the cells were epithelioid in appearance. Focal areas of hemorrhage and necrosis were present.

Fig. 3.

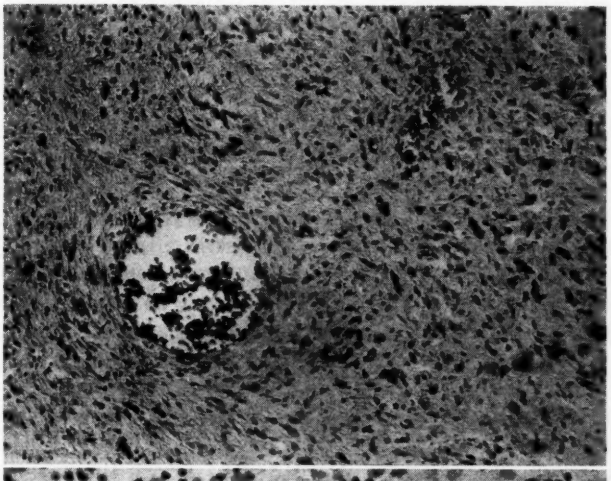

Fig. 4.

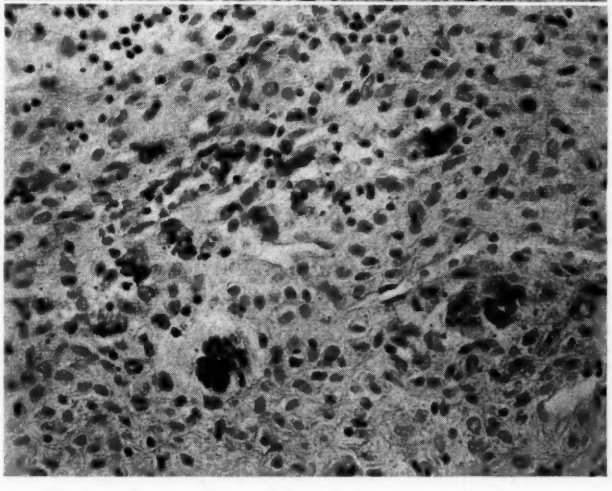

Fig. 3.—Section of metastatic lesion revealing alteration in cell structure. (×150.)
Fig. 4.—Higher-power view showing multinucleated cells. (×350.)

In two of eighty sections examined a few small collections of granulosa cells were noted (Figs. 1 and 2). Sections stained with Sudan IV revealed fine globules of intracellular fat. Corresponding areas revealed doubly refractile bodies present under the polaroscope.

*Grateful acknowledgment is made to Dr. Emil Novak for reviewing the material from this tumor.

Wilder's silver stain revealed a pericellular reticulum. A Masson stain failed to show muscle fibers.

Sections of the left broad ligament mass revealed a cellular tissue made up of epithelioid cells with fine reticular-like fibrils between the cells. Other portions were composed of interlacing spindle cells. Marked alteration in cell structure was present in many areas (Fig. 3). The nuclei were hyperchromatic and pleomorphic. Multinucleated cells were present (Fig. 4). Increased vascularity was evident.

Sections of the uterus, left ovary, and Fallopian tubes revealed a typical intramural fibromyoma and endometrium in the secretory phase. A corpus luteum was present in the left ovary. The Fallopian tubes showed no abnormalities.

Pathologic diagnosis: (1) malignant thecoma of the right ovary with metastasis to the left broad ligament; (2) fibromyoma of the uterus, intramural; (3) secretory endometrium; (4) corpus luteum, left ovary.

Review of the Literature

Loeffler and Priesel,[1] in their initial article on thecomas, included one they considered malignant. The tumor was present in a 67-year-old woman, para iv, whose chief complaint had been postmenopausal bleeding. At the time of surgery, 250 c.c. of peritoneal fluid was found. The left ovary was replaced by three tumors arising from a common stalk whose base was in the broad ligament. The tumor was adherent to the anterior abdominal wall. Two of the tumors were solid, measuring 8 by 7 by 5 cm. and 8 by 6 by 6 cm., respectively, and linked by a 3 cm. bridge. The third tumor was cystic, the size of a man's fist, and its wall was 1.5 cm. in thickness and yellow in color. The uterus and both adnexa were removed. Microscopically, the endometrium showed cystic hyperplasia. The two solid tumors revealed the architecture and cellular detail of a thecoma. The wall of the cyst in one portion was cellular, showed numerous mitoses and larger cells. On the basis of these microscopic findings, the peritoneal fluid and the adhesions, this tumor was considered malignant.

In 1937, Huber[10] reported a theca-cell tumor found in a 67-year-old woman, para ii, whose chief complaint was postmenopausal bleeding. At laparotomy the right ovary was replaced by a larger cystic tumor which contained a solid nodular portion. The cyst was the size of a man's head and the solid portion the size of a goose egg. The latter revealed areas which were yellow in color. Microscopically, the cyst was serous in type and the solid portion revealed the architecture and cellular detail of a theeoma. Areas in the solid portion, however, were very cellular, with numerous mitoses and some giant cells. The endometrium was hyperplastic. The tumor was considered malignant and the patient received external radiation.

In 1938, Geist and Gaines[11] published the report of a 49-year-old white woman, gravida 0, para 0, whose menopause occurred at the age of 47. Her presenting complaints were of two and one-half months' duration and included swelling of the abdomen, a 22 pound weight gain, constipation, occasional nausea and vomiting, anorexia and polydypsia. At operation, two quarts of serosanguineous ascitic fluid were removed. A large irregular right ovarian tumor was found, with numerous adhesions to small and large bowels. Many small metastatic nodules were seen scattered throughout the peritoneal cavity especially in the broad ligament and the posterior cul-de-sac. The adhesions were separated and the tumor removed. The neoplasm measured 21 by 20 by 14 cm. The surface was nodular. On section one portion was made up of solid, grayish-white tissue in which small yellow areas were interspersed. Cystic areas as well as portions composed of hemorrhagic, gray-brown tissue

containing large cavities were present. Microscopically, some of the areas were made up of plump spindle cells. In other areas the cells were epithelioid in character, markedly cellular with pleomorphism, mitotic figures, and variability in staining reaction. Some of these cells penetrated through the surrounding capsule. Numerous intracellular sudanophilic droplets were present which were doubly refractile. The diagnosis was malignant thecoma with metastasis.

A feminizing ovarian mesenchymoma with metastasizing theca-cell elements was reported by Carter and associates[15] in 1950. The patient was a 64-year-old woman, whose first symptom, bleeding, occurred twelve years after the menopause, in 1944. It continued at intervals for two years and was treated by diagnostic curettage. Progressive abdominal enlargement began. In March, 1946, a large cystic ovary was removed from the right side. Three years following this operation, the patient had ascites, and a large abdominal tumor. At operation a large cyst was found which was attached to the mesentery of the bowel and there were three metastatic encapsulated tumors. A subtotal hysterectomy and left salpingo-oophorectomy were performed, as well as excision of the metastatic nodules. One of these present on the sigmoid was removed by resection of the latter. Pathological examination of the original ovarian neoplasm revealed for the most part bundles of plump spindle cells containing lipoid material. In some areas it exhibited the cytologic characteristics of a granulosa-cell tumor. The metastatic nodules were of the theca-cell type, contained abundant intracellular lipoid and, as in the primary neoplasm, mitotic figures were fairly numerous. The endometrium was cystic and contained multiple adenomatous polyps. Final diagnosis was that of a metastasizing malignant theca-cell tumor.

Proctor and co-workers[12] in 1951 reported the case of a 52-year-old woman with a chief complaint of vague pelvic pain, and infrequent and scanty periods. The abdomen was swollen and tense. At operation, 2,500 c.c. of turbid gray fluid was present in the abdominal cavity. The entire peritoneal surface was thickened and covered with small papillary gray-white plaques. Both ovaries were enlarged, irregularly nodular, and adherent to the uterus. The mesentery and omentum were thickened. The patient died ten weeks after laparotomy. Surgical as well as postmortem material were available for study. The ovaries measured 5.5 by 4.5 by 3.5 cm. and 6.8 by 5.5 by 3 cm. Microscopic study of these showed interlacing bundles of spindle cells with vesicular nuclei and, in areas irregularly distributed throughout the stroma, masses of hyperchromatic cells with four to five nuclei in a cluster. The uterus removed at autopsy revealed atrophic endometrium. Postmortem histological studies showed metastatic tumor invasion of all muscle coats and submucosa of the stomach and intestines and extension to the peripancreatic tissue and myometrium. Sudanophilic areas were demonstrated in the ovaries and in the metastatic lesions. The diagnosis was malignant thecoma with metastasis.

Five thecomas have been reported as malignant, three on the basis of metastasis and two on the basis of somewhat inconclusive evidence. Loeffler and Priesel reported one of their thecomas as malignant because of ascites, adhesions, and a focal area in one portion of the tumor of increased cellularity, numerous mitoses, and variation in the size of the cells. Following the same criteria, Huber reported a malignant thecoma on the basis of increased cellularity, numerous mitoses, and the presence of giant cells. Admittedly the classification of these two neoplasms is difficult. Nevertheless, assigning them to the malignant group is somewhat premature. Until more information is collected as to what characteristics malignant thecomas possess, these two tumors should not be considered malignant.

Diddle,[16] in a review of granulosa- and theca-cell ovarian tumors, stated that three additional cases have been brought to his attention. Personal communication with him revealed that one case was found in the survey of female genital cancer in Dallas, Texas, made under the auspices of the American Cancer Society, Texas Division. Unfortunately the records are not available. The second case,[17] which has not been reported, is in a patient of Mengert. The third case was reported by Kottmeier.[18] A review of the original publication reveals that it was a broad ligament tumor described as a fibromatous granulosa-cell tumor with thecalike elements and a sarcoma-like appearance. Few mitoses were present. Both ovaries, however, were normal in appearance.

At the present time these cases cannot be included with the malignant thecomas.

Comment

Theca-cell tumors are usually benign but the incidence of malignancy cannot be definitely established. Including the present case there are four acceptable malignant thecomas reported so that the approximate incidence is 3 per cent. Since theca-cell tumors comprise 3 per cent of solid ovarian tumors,[3] malignant theca-cell tumors will be found only once in almost two thousand solid ovarian tumors.

Hyperestrinism is usually found in the presence of thecomas. Traut and Marchetti[13] have suggested that this endocrine activity is decreased by a lack of differentiation or high theca-cell content of the tumor. The absence of both atypical bleeding and hyperplasia of the endometrium in the present case is not unusual. Traut and Butterworth[14] have pointed out that the secondary hormonal effects are probably produced by its long-continued and unopposed action although the amount secreted may be small. In our case this action was opposed by apparently sufficient secretion of progesterone from a corpus luteum present in the opposite ovary to produce a secretory endometrium.

There are an insufficient number of thecomas to evaluate properly the correct method of therapy. At the present time, however, surgical removal is the method of choice. In young women the tumor can probably be removed with preservation of the other pelvic organs. In the older patient, panhysterectomy is advisable because of the increased incidence of endometrial carcinoma associated with feminizing mesenchymomas,[9] as well as the malignant potentialities of the tumor. Little is known about the radiosensitivity of these tumors. The experimentally produced tumors in the mouse are radioresistant. Postoperative radiation is advised in the treatment of malignant thecomas.

Summary

A case of malignant thecoma has been presented. Five previously reported cases have been reviewed and only three of these have criteria acceptable for malignant tumors. The incidence of malignancy in theca-cell tumors is approximately 3 per cent.

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THE DIAGNOSIS OF VERY EARLY CARCINOMA OF THE UTERINE CERVIX DURING PREGNANCY*

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WE BELIEVE that pregnant women offer favorable opportunity for detection of incipient cancer of the cervix uteri and will present material in support of such opinion. This is based on discovery of one very early malignancy by random biopsies of friable or bleeding cervical erosions among 2,000 pregnancies[1]; and one early invasive growth, plus one questionable carcinoma in situ from 1,600 cytological screenings[2] previously reported. To this we now add a small new series of 500 Papanicolaou cervical smears showing 3 highly suspicious cervical lesions but no cancer.

There are certain difficulties in the search for early cancer of the cervix during pregnancy which are responsible for much skepticism concerning the value of such effort. The most important criticisms are: (1) infrequency of cervical cancer in relatively young age groups; (2) gross and microscopic changes in the cervix during pregnancy frequently simulate early malignancy; (3) limitations of cytologic cervical smears and unreliability of single smear tests for screening purposes; (4) inability to secure safely really adequate biopsy material such as complete sharp or cold cervical conization, due to risk of hemorrhage. These four questions will be discussed in order.

Our two cervical malignancies, one questionable carcinoma in situ, and three suspicious cases were all in multigravidas averaging 31 years of age and parity iv. However, there is ample evidence to indicate variable prolonged dormant stages of both preinvasive and invasive cervical cancer.

Nearly one-half of all of our patients showed gross cervical lesions, mostly simple, elevated, papillary or polypoid "erosion," generally friable, including many polyps and some condylomas, all of which were biopsied and a few found to be decidual. If we add to the above features, bleeding from threatened abortion, cervical discharge, and vaginal exudate due to frequent *Trichomonas vaginalis* or mycotic vaginitis, it is obvious that neither subjective symptoms nor simple inspection provides reliable basis for suspecting cancer.

Microscopic diagnosis of preinvasive cervical cancer during pregnancy can be positive after multiple expert opinions or prolonged postnatal observations or both, but early invasive cancer can be determined immediately. Biopsy diagnosis of carcinoma in situ from the nonpregnant cervix is difficult, as shown by Novak and Galvin,[3] who reported 25 cases not confirmed after operation. Error in these cases was attributed to misinterpretation of varying degrees of basal-cell hyper-

*Read at a meeting of the Philadelphia Obstetrical Society, March 6, 1952.

activity. Diagnosis of preinvasive or preclinical epidermoid cervical carcinoma during pregnancy is more difficult, due to the following frequently confusing microscopic features: (1) marked proliferation of the endocervix in healing erosions[4]; (2) epidermization[5] (14 per cent) and adenomatous glandular hyperplasia simulating neoplastic process; (3) decidual reaction (10 to 20 per cent); (4) hyperactivity of basal cells (20 per cent). Epperson and collaborators[6] found that 85 per cent of pregnant cervices showing basal-cell hyperactivity had returned to normal by the fourth postpartum week, and all of 5 cases of histologic "carcinoma in situ" showing apparently typical nuclear hyperchromatosis, active mitosis, and loss of polarity, marked anaplasia, and even questionable invasion of the basement membrane.

However, it is important to note that recently it has been proved[7, 8] that while confusing microscopic epithelial changes of the cervix are more common during pregnancy, they are not specific. In other words, if the criteria of preclinical or preinvasive epidermoid carcinoma are present, these criteria are valid whether or not the patient is pregnant, although in the case of carcinoma in situ we believe that prolonged postnatal observation should be elected to verify the diagnosis.

The general limitations of Papanicolaou cervical smears are well known, but there has been insufficient usage in pregnancy to permit positive conclusions to date. Cuyler and associates[9] from 1,451 pregnancy smears found 206 examples of atypical cytology (13.5 per cent) including 17 (1.2 per cent) intraepithelial carcinomas, and concluded that properly secured smears portray to a very high degree abnormal microscopic processes. To this we agree and add that a first or single smear is usually sufficient for screening purposes.

Haynes and co-workers[10] also reported a large number of routine vaginal cytological screenings from pregnant women among 6,816 patients of various groups tested by combined cervical aspiration and spatula spreads. Thirty-six of these (0.53 per cent) patients showed 13 unsuspected invasive cervical carcinomas and 23 preinvasive.

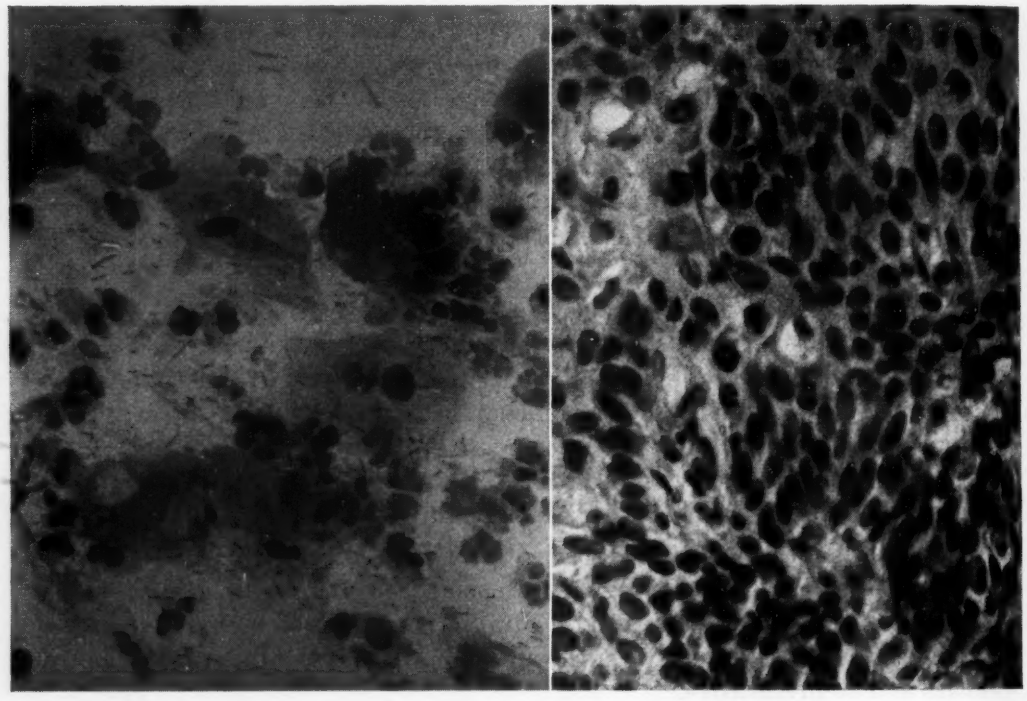
The chief limitation in search for early cervical carcinoma in pregnancy is inability to secure complete circular biopsy of the squamocolumnar junction without serious hemorrhage. Therefore, all of our suspicious and positive smear cases, plus cases of polyps, condylomas, and exceptionally friable erosions, regardless of smear results, were checked only by one or more punch biopsies, without excessive bleeding, abortion, morbidity, or other complication. Epperson and his associates[6] performed 286 antepartum cervical biopsies resulting in only one hospitalized case of hemorrhage, so we may conclude that cervical punch biopsies are safe, but incomplete, and at the present time cytologic screening is the only practical approach to the problem of finding early cancer of the cervix in pregnancy.

Material

Our third series of 530 Papanicolaou cervical smears were taken routinely from all pregnant women registered in Preston Maternity Hospital, and examined

through the courtesy of A. Reynolds Crane, M.D., Director, and Allan D. Wallis, M.D., Assistant Director, the Ayer Clinical Laboratory, Pennsylvania Hospital. The series is small but permitted individual critical examination by one or both of the authors, who also secured all spatula smears and biopsies.

Table I is self-explanatory. Table II shows 2 cases in which there were suspicious prenatal smears, but the patients moved elsewhere and cervical biopsies could not be obtained. One of the three women showing positive smears (Mrs. R. H.) appeared to have typical carcinoma in situ during her pregnancy but was allowed to proceed to normal delivery and repeated abnormal postnatal observations according to the summarized case history given below.



A. *B.*

Fig. 1.—Mrs. R. H., pregnancy. *A*, Positive cervical smear, and *B*, "Carcinoma in situ," proved nonmalignant after hysterectomy sterilization.

Table III is of special significance in that one of the 3 patients with positive smears during pregnancy (Mrs. E. F.) showed abnormal smears and biopsies 31 weeks after delivery, which should be considered "precancerous," and will be followed indefinitely. (See summary.)

Table IV includes only a few gelatin sponge cervical "biopsies," many of which were inadequate, had to be repeated, and were discontinued as likely to yield false-negative screening. Thirteen of the 17 suspicious smears listed in Table V were judged to be in Class III, but we believe that grouping of abnormal smears as suspicious or positive for tumor cells is sufficient and preferable to "Classes." The results tabulated in Table V are final conclusions, showing rather less early cervical cancer and much less carcinoma in situ than appears in reports that have followed our original preliminary study published in January, 1950.

TABLE I. RESULTS OF LATEST (THIRD) SERIES OF PAPANICOLAOU CERVICAL SMEARS

Pregnancy smears		530
Negative	519	
Suspicious	8	
Positive	3	

TABLE II. THREE "FALSE POSITIVE" SMEARS AMONG 530, OR AN INCIDENCE OF 0.57 PER CENT

PREGNANCY CERVICAL BIOPSIES:		
Suspicious smear cases		8
Chronic cervicitis	4	
Cervical polyp	1	
No pathology	1	
Unavailable	2	
Positive smear cases		3
Chronic cervicitis	2	
Carcinoma in situ (Mrs. R. H.) (later disproved)	1	

TABLE III. ALL OF THE 3 POSITIVE PRENATAL SMEAR CASES SHOWED POSITIVE OR SUSPICIOUS SMEARS AND ABNORMAL BIOPSIES FROM 1 TO 31 WEEKS POST PARTUM

POSTNATAL BIOPSIES		
Suspicious smear cases		8
No pathology (smears negative)	3	
Cervical polyp (smear negative)	1	
Not available	2	
Undelivered	2	
Positive smear cases		3
Chronic cervicitis (Mrs. R. H.) (Smear positive)	1	
Chronic cervicitis, marked squamous hyperplasia (Mrs. E. F.) (Smear positive)	1	
Squamous-cell activity (Mrs. T. S.) (Smear suspicious)	1	

TABLE IV. SCREENINGS INCLUDE 235 GELATIN SPONGE CERVICAL "BIOPSIES" AMONG THE SECOND SERIES

Previously reported screenings	
First series	222
Second series	1,404
Present series	530
Grand total	2,156

TABLE V. TOTAL SMEARS AND SPONGE BIOPSIES—2,156

Negative	2,131	
Suspicious		21
No tumor	20	
Cancer (proved)	1	
Positive		4
No tumor	3	
Questionable	1	

Case Reports

CASE 1.—Mrs. R. H., aged 36 years, para ii, gravida iii, was sensitized to the Rh factor, and had arrested pulmonary tuberculosis. The last menstrual period was April 21, 1950. She was asymptomatic, with a lacerated cervix, and elevated erosion one plus.

10-11-50: Cervical smear, suspicious.

10-25-50: Biopsy, epidermoid carcinoma of cervix.

11- 8-50: Cervical smear, positive for tumor cells.
12-13-50: Biopsy, squamous metaplasia; pregnancy changes.
1- 3-51: Delivered spontaneously at 37 weeks, erythroblastotic infant.
2-24-51: No symptoms; large, soft cervix with one plus simple erosion; small uterine myoma; cervical smear, positive for tumor cells; biopsy, chronic cervicitis, squamous metaplasia.
4- 4-51: Smear, positive for tumor cells.
4-13-51: Smear, suspicious for tumor cells.
4-25-51: Total abdominal hysterectomy, bilateral salpingo-oophorectomy, chronic cervicitis with squamous metaplasia.
6- 1-51 and 12-21-51: Condition good.

CASE 2.—Mrs. E. F., aged 27 years, para viii, gravida ix, had her last menstrual period Oct. 16, 1950. She had a heavy yellow vaginal discharge, no bleeding; a lacerated cervix, simple erosion one plus, eversion.

3- 4-51: Cervical smear, positive for tumor cells.
4- 6-51: Cervical biopsies, chronic cervicitis with squamous metaplasia.
7-12-51: Delivered spontaneously at term.
2-21-52: Follow-up delayed by patient; normal menses, discharge; large, lacerated, nodular cervix. Cervical smear, positive for tumor cells. Biopsy, chronic cervicitis with marked squamous metaplasia.

CASE 3.—Mrs. T. S., aged 32 years, para vi, gravida vii, had her last menstrual period May 12, 1951. She had a constant dark vaginal discharge, occasionally bloody since the third month of pregnancy. Cervicovaginitis with papillary erosion one plus.

12-26-51: Cervical smear, positive for tumor cells.
1-11-52: Cervical biopsies, chronic cervicitis with Nabothian cysts.
2-20-52: Delivered spontaneously at term.
2-27-52: Cervical smear, highly suspicious for tumor cells. Biopsies, epithelial activity, no malignancy.

Comment: Are the time, effort, and expense involved reasonable in the light of the relative infrequency of cervical carcinoma in pregnancy? This question can be answered in the affirmative provided the most expert pathological opinion is available. For example, one case of unsuspected cervical cancer was found in a total of 2,153 smear screenings, whereas, without smears, in over 20,000 registered ward pregnancies, only one cervical carcinoma (Stage III) was found in Pennsylvania Hospital.

Conclusions

1. Cytological smear screening is reasonably accurate for diagnosis of early carcinoma of the cervix during pregnancy.

2. Many thousands of such tests will be required to establish precise percentages of false-negative and false-positive readings.

3. Diagnosis of preinvasive carcinoma of the cervix in pregnancy should be verified by repeated postnatal observations rather than by interruption of pregnancy.

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Discussion

DR. J. ROBERT WILLSON.—As compared to some other conditions, carcinoma of the cervix in pregnancy does not constitute an important cause of death, but if the figure of one cancer in every 2,000 pregnancies as reported here is correct approximately 1,900 new malignant lesions of the cervix should have been discovered in 1951. In addition most of the 1,900 tumors should have been in such an early stage that their complete eradication would have been possible. Unfortunately, few of these carcinomas were detected because careful examinations directed toward the diagnosis of cancer were not made. In addition the reliable screening techniques utilized in this study are not as yet generally available and therefore cannot be made use of as part of the initial examination of all pregnant women.

Despite the over-all figures, it is difficult to persuade the physician who delivers 100 women annually that a lesion he will encounter once in 20 years is important, but if the prenatal examination is carefully planned and properly carried out these early lesions can be found by any doctor. Exposure of the cervix, its careful inspection in a good light, and collection of material directly from the squamocolumnar junction are the first important steps. Such careful technique, however, is valueless unless the spread is properly processed and examined. Although most commercial laboratories are willing to perform cytologic examinations, it is questionable whether or not the results of such studies are reliable. A positive diagnosis can usually be made rapidly but every cell on a negative spread must be inspected and the time involved for the examination of multiple normal smears is more than can be expected on a commercial basis. The normal changes in the cervical epithelium during pregnancy, cervicitis, and other genital-tract lesions are often so difficult to differentiate from malignancy that they tax the ability of the most expert cytologists. Best results can be obtained if the carefully collected material is prepared and examined by an individual trained and experienced in cytologic diagnosis. Furthermore, the cytologic report must be interpreted in relationship to the clinical findings, the duration of pregnancy and the presence of other pelvic abnormalities. The acceptance of a diagnosis of malignancy from the smear without confirmation by microscopic examination of cervical tissue is even more hazardous during pregnancy than in nonpregnant women and treatment must not be administered unless an unequivocable diagnosis of cancer can be made. I am in complete accord with the authors' advice that a decision as to the need for treating an intraepithelial carcinoma diagnosed during pregnancy must be delayed until adequate postpartum evaluation is possible.

While the technique described in this paper will undoubtedly reveal almost all cervical cancers in pregnant women such careful evaluation is not always possible. Until facilities for accurate cytologic study are more generally available physicians must rely upon the usual methods of examination. Careful inspection of the cervix through a speculum will reveal any ulcerated, hypertrophic, or friable lesion which must then be biopsied. Multiple punch biopsy rather than complete removal of the squamocolumnar junction is preferable due to the extreme vascularity of the cervix. This procedure usually may be done in one's office since it is painless and hemorrhage which cannot be controlled by a vaginal tampon is infrequently encountered. While lesions found by this method may well be somewhat more advanced than those detected by cytology they usually are relatively early and offer a favorable prognosis for treatment. It is hoped that in the future the methods described in this paper will be generally available and that every physician who cares for obstetric patients will use them intelligently, thus preventing the needless loss of life from delayed diagnosis of malignancy.

DR. GEORGE A. HAHN.—With a patient who is pregnant and has infection coincident with pregnancy one can find spreads which in nonpregnant women would be doubtful. Great caution must be exercised in these smears in pregnancy so that false diagnosis is not made. The experience at Jefferson is showing in which cases biopsy can be done. There was one patient under our care in 1946, 20 years old, with a prominent granular erosion of the cervix, interpreted as being suspicious of malignancy. Biopsy was taken and reviewed by a number of pathologists and seen by Dr. Novak, whose opinion was that despite the youth of the patient, he could make no other diagnosis than carcinoma in situ. That was in February, 1946. Because of this, extensive biopsy was done in March which showed thickening of superficial tissues. She was the subject of much discussion. Cesarean section was advised. The patient had refused any treatment of the cervix because her husband was away. She was delivered of a healthy child. After the uterus had involuted, examination was repeated and showed no evidence of malignancy, just a healing erosion. Since that time the patient has been seen at intervals. She has no symptoms and has an intact, well-healed cervix. Our feeling is that when diagnosis of carcinoma in situ is made one must be exceedingly cautious, and doubly so when the diagnosis is made in pregnant women.

DR. HIRST (Closing).—I think we all agree that cytologic screening is not a universally available test, but it should be continued to establish certain facts with regard to carcinoma during pregnancy. A conservative attitude with regard to carcinoma in situ is proper.

TECHNICAL IMPROVEMENTS IN CULDOSCOPIC EXAMINATION

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THE first attempt to visualize the abdominal viscera was made by Kelling in 1903 with a Nitze cystoscope through the anterior abdominal wall. It was not until 1940, however, that Te Linde entered the cul-de-sac with a modern peritoneoscope to inspect the pelvic organs. In 1942 Decker applied the knee-chest position to culdoscopic examination and thereby avoided a major obstacle, the intestines.

It is now generally recognized that culdoscopic examination is an important aid to gynecological diagnosis in selected cases. Many gynecologists are still reluctant to use culdoscopy as frequently as it may be indicated. This attitude has been justified, at least in part, by the following reasons:

1. There was no simple and adequate anesthetic method to prevent pain, enable the patient to maintain the knee-chest position without special equipment and several interns or nurses to hold her, and, finally, provide the surgeon with relaxation and exposure sufficient to assure the success of the procedure.
2. The postoperative discomfort, pain, nausea, etc., were quite distressing.
3. There was a significant number of failures to enter the peritoneal cavity.

During the past two years we have performed 128 culdoscopic examinations, largely in private patients. Our results indicate that we have apparently overcome these difficulties.

Anesthesia

We have considered all the possible anesthetic techniques and tested several. We are now satisfied that the special needs of a culdoscopic examination and the specific characteristics of the patient for culdoscopy are the best served by the use of spinal analgesia with a hypobaric solution of 20 mg. of Lucaine Hydrochloride* in 3 c.c. of distilled water administered through a 26 gauge spinal needle. The anesthetic demands peculiar to a culdoscopic examination are the following:

1. The analgesia should cover the zone innervated by the sacral, lumbar, and lowest thoracic nerves to prevent completely any discomfort during manipulation of the pelvic organs, especially if these are diseased or painful before culdoscopy. A "saddle block," truly confined to the lumbosacral area, is inadequate for complete analgesia.

*Lucaine Hydrochloride was supplied by the Maltbie Laboratories, Newark, N. J.

2. The patient should retain voluntary motor power to be able to maintain the knee-chest position. Although she may be aided by straps binding her thighs to the vertical posts of leg holders, she should not require any other assistance in holding her position. The abdomen should be relaxed and free to expand; any abdominal support or contraction interferes with the development of maximum intra-abdominal negative pressure and a large pneumoperitoneum after puncture of the vaginal vault in the knee-chest position.

3. The intestinal tract should be maximally contracted and retracted to minimize the chance of accidental puncture and to permit optimal visualization of the pelvic organs.

4. The anesthetic technique must have a mortality of zero to be safe as the diagnostic procedure itself.

The particular characteristics of the patient for a culdoscopy are:

1. She should be able to leave the hospital on the same day if desired. Since culdoscopy is primarily performed for diagnosis, early ambulation and discharge from the hospital are important.

2. The patient is frequently hypersensitive or emotionally unstable. The utmost care is necessary, therefore, to fulfill the assurance that the examination is not too uncomfortable and is not followed by distressing complications.

3. The patient may again require anesthesia on the same day or subsequently for a surgical procedure as indicated by the culdoscopic findings. The anesthesia for a culdoscopy should not condition her against a subsequent operation. We are particularly interested in avoiding pain during the examination and postpuncture headache.

The pioneer work of Decker was performed with local anesthesia. Te Linde and others have also used local anesthesia. This was the safest method available to these investigators and it is still the method of choice of those who cannot give their patients the protection afforded by the services of an anesthesiologist. With local anesthesia heavy premedication is necessary; it often interferes with the muscular control of the patient. Dissatisfaction with local anesthesia, after extensive experience with it, is the primary reason for Decker's current preference for spinal anesthesia.

General anesthesia has been employed by Te Linde. This method is somewhat awkward and hazardous in a patient in the knee-chest position unless an endotracheal airway is in place. Intestinal dilatation and vomiting during culdoscopy may result, and increase the danger of perforation of the intestines. The postoperative discomforts and disadvantages of general anesthesia delay early self-care and prolong the hospital stay. We have not used general anesthesia because it is a major anesthetic method for a minor gynecological procedure.

Epidural analgesia by the caudal or lumbar route has been tested on several occasions. It has been an ideal method in a few instances and remains in our armamentarium as a good second choice. In some cases, however, we have found it unreliable for the following reasons:

1. Sacral anomalies and pilonidal sinuses sometimes prevent the caudal approach from being available.

2. Caudal analgesia may fail to rise sufficiently cephalad to permit a completely painless culdoscopy. Lumbar epidural analgesia may fail to descend to include the lowest sacral nerves. Epidural analgesia requires a 20 minute waiting period and then one may unexpectedly fail to have bilateral spread of analgesia. The unique advantage of epidural anesthesia, e.g., the avoidance

of neurological sequelae to lumbar puncture or spinal anesthesia, loses its significance when it is appreciated that these sequelae have also been avoided by our technique of spinal anesthesia.

Spinal anesthesia is the current choice of Decker, Decker, and Milowsky,[1] and of Shanafsky and Ziemba.[2] We have modified the method and prefer the following technique:

Lumbar puncture is performed with a 26 gauge, 10 cm. spinal needle passed into the subarachnoid space through a 21 gauge, 5 cm. needle previously inserted to but not through the dura as an introducer. This "double-needle" technique has been described in detail in another report.[7] The minute opening left in the dura by a 26 gauge needle permits so little postpuncture leakage of spinal fluid that the typical postpuncture headache is rare. If, in addition, the patient is ordered to drink ten glasses of fluid (300 c.c.) a day for three days, a postpuncture headache is encountered even more rarely. Decker, Decker, and Milowsky reported only one severe headache in 25 patients with the use of a 20 gauge needle. Shanafsky and Ziemba had no complications following puncture with a 20 or 22 gauge needle in 57 patients at a U.S. Marine Hospital. We have not encountered a headache in our series of 128 culdoscopic examinations performed with the 26 gauge needle. These three groups are too small, however, to be of statistical significance in evaluation of the effect of any single factor in the occurrence of a postspinal headache. Proof of the superior value of the 26 gauge needle and force hydration has been established in larger groups of patients given spinal anesthesia for vaginal delivery; these studies have been published elsewhere.[7]

The other significant feature of our technique is the use of Lucaine Hydrochloride in hypobaric solution. Lucaine is a relatively new anesthetic drug which is effective in small doses. It lends itself, therefore, to the preparation of a hypobaric solution, e.g., 20 mg. of Lucaine Hydrochloride crystals in 3 c.c. of distilled water. A hypobaric anesthetic solution is especially suitable for culdoscopic examination because it permits the patient to assume the knee-chest position immediately, with the expectation that the posterior roots in the lower spinal canal will be predominantly affected. In this way we have regularly produced excellent analgesia to T_{-10} without loss of motor power in the lower extremities and back.

A similar purely sensory block can be produced with appropriate concentrations and doses of other anesthetic agents and is not a specific characteristic of Lucaine as pointed out by Conner and Dripps.[6] Milowsky[1] has obtained the same result with 25 to 50 mg. of procaine in a 2.5 per cent solution but the analgesia could be depended upon for only 20 minutes. Lucaine, 20 mg. in 3 c.c. distilled water, has regularly afforded us an hour of analgesia and has allowed culdoscopy to be used for teaching or photography. We have also tried Pontocaine, 2.5 to 5 mg., in 0.1 per cent solution using 0.25 to 0.5 c.c. Pontocaine fluid in spinal fluid, distilled water, or 10 per cent glucose. These solutions, with appropriate changes in position, were not dependable in producing a purely sensory effect. A smaller concentration or dose of Pontocaine reduced the reliability of obtaining effective analgesia to T_{-10} for the required minimum of 30 minutes.

A vasopressor drug, ephedrine sulfate, 50 mg., or preferably Neo-Synephrine chloride, 5 mg., is administered hypodermically before spinal puncture. Although the head-down aspect of the knee-chest position tends to maintain the arterial blood pressure, nevertheless, it frequently falls during the culdoscopic examination or immediately after it unless a vasopressor agent is used. The hypotensive tendency is caused by the block of lumbar and thoracic sympathetic pathways, the position of the thighs and legs in hindering

venous return and, sometimes, by a traction reflex from a vigorously pulled cervix.

Postoperative Course

The postoperative course of 128 cases was studied. These patients were divided into two groups.

Group I.—These patients, upon completion of the examination, were placed on the side with the trocar still inserted and the air expressed as far as possible by exerting pressure on the abdomen and flanks.

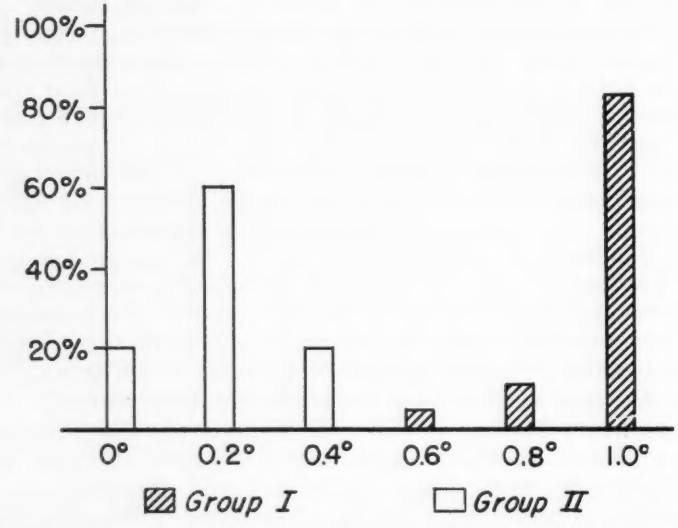

Fig. 1.—Temperature elevation 12 to 24 hours after culdoscopy in Groups I and II.

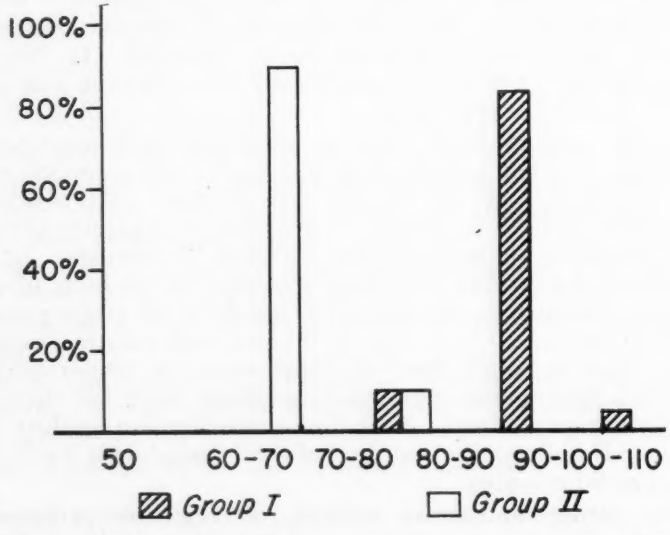

Fig. 2.—Pulse rates in both groups 12 to 24 hours after culdoscopy.

Group II.—In these patients, upon completion of the examination, a 20 F. catheter was introduced through the trocar and the trocar was removed. The patient was placed on her side and the air expressed as in Group I. The end of the catheter was then plugged with an ampule and left in position for four to eight hours with the cul-de-sac puncture thus sealed.

In all of the patients of Group I the abdomen was distended to a varying extent. There was tympanism and the patients complained of pain in the shoulders and abdomen, especially on breathing. In a number of patients there were nausea and general malaise. The patients in Group II, however, exhibited little or no distention, or tympanism, or shoulder pain, or pain on breathing; there was no nausea or vomiting.

Figs. 1 and 2 show the temperature and pulse rates of the two groups. The morbidity rate, as evidenced by pulse rate and temperature elevation, is far greater in Group I than in Group II.

It appears to us that a certain amount of air remains in or enters the peritoneal cavity through the cul-de-sac puncture after the completion of the procedure, even though the air was presumably expressed thoroughly. This was borne out by x-ray examinations of patients of each group revealing the amount of air present under the diaphragm in representatives of both groups. Group II patients exhibited a far smaller amount of air under the diaphragm than those in Group I.

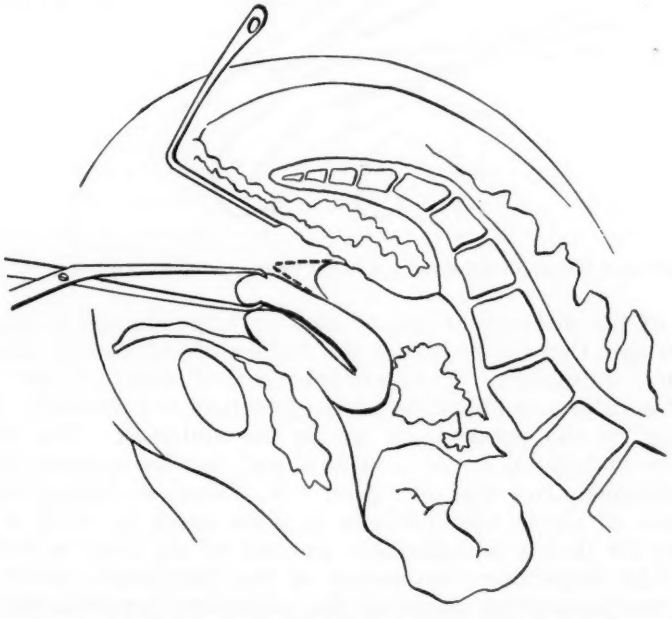

Fig. 3.—Showing the V shape of the cul-de-sac and the effect of the pull upon the cervix (dotted line).

Failure to Enter the Peritoneal Cavity

Anatomical Considerations.—The point of entrance into the peritoneal cavity of the pelvis is described as a point between the posterior aspect of the cervix and the ampulla of the rectum. The posterior lip of the cervix is grasped with a tenaculum and pulled down while a Sims speculum pulls up the posterior wall of the vagina, thereby permitting air to enter and distend the vagina.

A cross section of the female pelvis (Fig. 3) shows the cul-de-sac as a V-shaped excavation. When pull is exerted on the posterior lip of the cervix, the angle of the V becomes more acute; hence, thrusting a trocar into that space may often penetrate the mucosa and overlying fascia but will slide either posteriorly or, more likely, anteriorly along and within the areolar space of the subperitoneal tissue. This has occurred on ten occasions.

To avoid this, we have placed an Allys clamp about 2 cm. posterior to the cervix and put the mucosa on stretch by firmly pulling on it. The point of entrance is then chosen at about 0.5 cm. below the insertion of the clamp. Fig. 4 demonstrates these anatomical relations. This procedure is not always necessary, but whenever the uterosacral ligaments are long and attenuated, thereby not permitting the posterior vaginal vault to be stretched, this procedure may be of help. This method was used four times after initial failure to enter the peritoneal cavity and six times on patients with attentuated uterosacral ligaments.

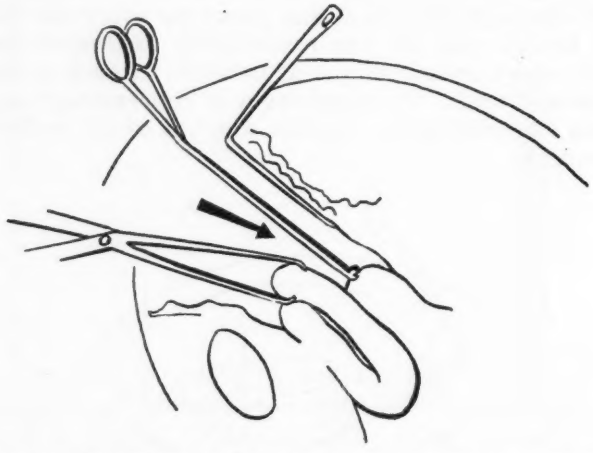

Fig. 4.—Demonstrates the application of the Allys clamp, putting the posterior vault on stretch.

The use of the instrument (tenaculum or Allys clamp) is helpful in entering the cul-de-sac, thereby reducing the failure of culdoscopy due to technical difficulties to a minimum. The postoperative discomfort and pain, the increase in pulse rate, and elevation of temperature are probably due to peritoneal irritation by the presence of air in the abdomen. The placing of the catheter in the abdominal cavity acts as a seal for the opening and no air will enter the abdomen after the operation. A plausible explanation for the increased volume of air in the abdomen in those cases in which a catheter was not used may be that a considerable amount of air may be sucked into the abdomen by the respiratory movement of the diaphragm while the valvelike behavior of the punctured tissue of the cul-se-sac prevents the expulsion of the aspirated abdominal air.

Summary and Conclusions

1. One hundred twenty-eight culdoscopic examinations in 124 patients have been performed.

2. Various methods of anesthesia are discussed. Our choice is spinal analgesia to T_{-10} with the use of 20 mg. of Lucaine Hydrochloride in 3 c.c. of distilled water injected through a 26 gauge lumbar puncture needle.

3. This study shows the value of placing a sealed catheter into the cul-de-sac immediately after the examination has been completed and the air expressed from the abdomen.

4. Failure to enter the abdominal cavity has been discussed and our method of avoiding failure presented.

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USEFULNESS OF THE BASAL METABOLIC RATE IN PREGNANCY

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THE basal metabolic rate in pregnancy has been the subject of considerable investigation since Magnus Levy's first report in 1897. Interpretation and explanation of the findings, however, have been varied and remain controversial. Much of the work of the past was summarized by Javert[1] in 1940, with a graphic composite of the findings of Baer, Sandiford and Wheeler, Plass and Yoakam, Hughes, Hanna, and Colvin and Bartholomew in the form of a probable basal metabolic rate curve in normal pregnancy'' (Fig. 1).

During the first weeks of pregnancy, the metabolic rate is not remarkable. At approximately the twenty-second week, a very definite rise appears. This rise has been explained in at least three different ways, and no explanation is entirely satisfactory. Sandiford and Wheeler[2] believe that it is due to the increase of protoplasmic mass, the rise in BMR being proportional to the combined masses and surface areas of the mother and fetus. In other words, they believe that the rate of metabolism per unit of tissue is not increased. This view has been questioned, however, by Rowe and Boyd,[3] who challenge the basis of Sandiford's and Wheeler's calculations; but Rowe and Boyd are themselves unable to explain the change in BMR. As further evidence against the explanation of Sandiford and Wheeler, Javert points out in his series of eighteen hyperthyroid patients that the BMR was essentially the same in the last two trimesters and in the postpartum period. This observation, he believes, is against the explanation of elevation of BMR on the basis of increased protoplasmic mass of mother and fetus.

A second explanation is that the rise in the basal metabolic rate in the latter half of pregnancy is secondary to thyroid hyperplasia. In support of this explanation has been offered the palpable enlargement of the thyroid gland occurring in many pregnant patients (40 per cent according to Hanna[4] and up to 80 per cent according to others). Another argument along this line has been suggested by Javert, who, reasoning from his cases of hyperthyroidism, explains the rise in BMR on the basis of thyroid hyperplasia. Since the enlargement of the gland occurs chronologically well in advance of the rise in BMR, this argument for hyperplasia as the explanation seems quite untenable. Furthermore, experimental work by Peters, which will be mentioned later, is definitely against increased thyroid activity as an explanation.

A third explanation, unrelated to thyroid activity, is offered by Zunty (cited in DuBois[5]) who stated that the rise, in part at least, represented the additional work imposed by interference of the enlarging uterus with the mechanics of respiration.

†Deceased, Feb. 27, 1952.

It is of some interest also that Sontag and associates,[6] in studying the relation of the basal metabolic gain during pregnancy to basal metabolism in the nonpregnant state found, generally speaking, that women with low nonpregnant levels show a greater than average gain, usually in the latter months. A possible explanation was offered on the basis of a typical hypersensitive response of a hypothyroid mother to the thyroid of her fetus with a possible fetal compensatory hypersecretion.

Although the BMR during pregnancy has been the subject of considerable interest, little attempt known to us has been made to correlate the results of this test with other aspects of pregnancy, although its use in the prevention of abortion is frequently cited. Since the thyroid hormone is known to be essential for normal maturation, menstruation, and the maintenance of pregnancy and is believed to determine the rate of the organism's metabolism, a study to determine whether there exists in pregnancy any correlation between slow or rapid metabolism and (1) spontaneous abortion rate, (2) weight gain during pregnancy, (3) duration of pregnancy, (4) the sex, and (5) birth weight of the offspring seems definitely justified.

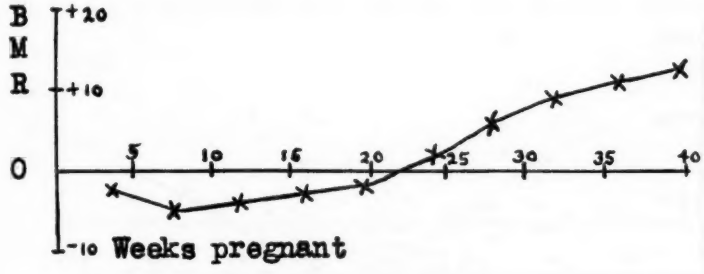

Fig. 1.—After Javert.[1]

Materials and Methods

The present study was undertaken with these objectives in mind. A single BMR was taken under standard conditions at either of two local commercial clinical laboratories, usually within ten days of the patient's first prenatal visit. In the event that the laboratory reported a test to be unsatisfactory, the case was not included. Two groups of patients were studied.

Group I consisted of 100 consecutive patients, none of whom were taking thyroid when first seen. There were, in this group, 81 multigravidas and 19 primigravidas. The age range was 18 to 40 years; and the time of the BMR tests ranged from the sixth through the thirty-ninth week of gestation. It was ultimately found, after the 100 patients had been collected, that all the pregnancies were clinically normal at the time of the first prenatal visit.

In the analysis of the material from Group I, a normal BMR has been interpreted as one within the range of 10 per cent below and 10 per cent above the average BMR for the week of gestation in which the test was made. As is shown below, this average BMR varies considerably from the usual zero base line.

Group I was studied for: (1) average BMR during pregnancy, (2) range of BMR during pregnancy, (3) possible correlation of present BMR and past history of spontaneous abortion, (4) possible correlation of BMR and threatened abortion, (5) clinical effect of thyroid, if given.

Group II consisted of 50 consecutive clinically normal primigravidas whose pregnancies were known to have terminated successfully. The age range was 17 to 38 years and the time of the BMR tests ranged from the eighth through the thirty-eighth week of gestation.

Group II was studied after an average curve was obtained. The patients were divided into three classifications: (1) normal; (2) BMR more than 5 per cent above the average; and (3) BMR more than 5 per cent below the average for the week of gestation in which the test was made. The three classes were then compared as to: (1) length of pregnancy (number of days from LMP), (2) average weight gain of the mothers, (3) average weight of the offspring, and (4) sex of the offspring.

Results

Group I.—The range from plus 37.5 per cent to minus 23.5 per cent and average curve obtained are shown in the scattergraph in Fig. 2. Sixty-four were in the normal range; 18 were more than 10 per cent above normal; and 18 were more than 10 per cent below normal. Table I summarizes the material regarding abortion and the use of desiccated thyroid.

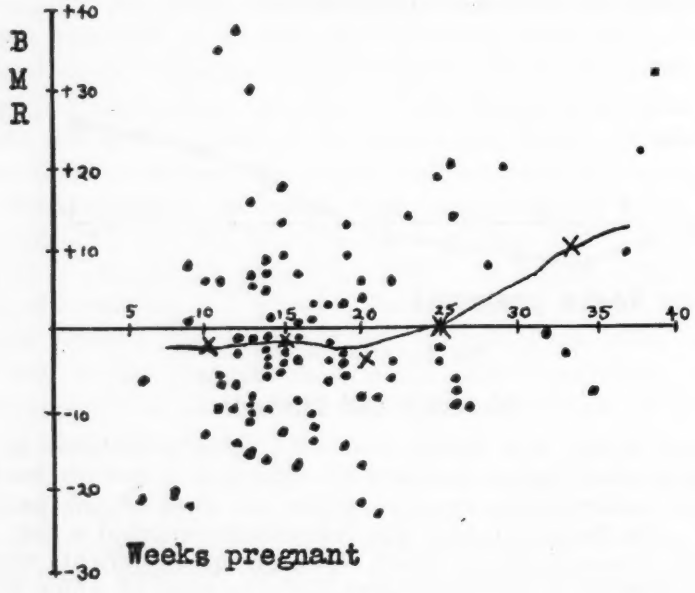

Fig. 2.

Among the 81 multigravidas, there were 17 with a total of 19 previous spontaneous abortions. Of these 17, 7 were patients whose BMR fell within the normal range; 5 were patients with the BMR above the normal range; and 5 were patients with the BMR below normal range. (Normal range is defined as within 10 per cent above to 10 per cent below the average BMR for the week of gestation in which the test was made.)

TABLE I

	TOTAL	NORMAL BMR	ELEVATED BMR	SUBNORMAL BMR
Group I	100	64	18	18
Previous abortions	17	7	5	5
Threatened abortions	12	6	4	2
Treated with desiccated thyroid	21	10	-	11

There were 12 cases of threatened abortion during the current pregnancies. Six occurred in patients with BMR within the normal range; 4 in patients with BMR above normal range; and 2 in patients with BMR below normal range. Only one of the 2 patients with both threatened abortion and the BMR lower than normal was given thyroid; both have delivered normal term babies. Most of the patients with threatened abortion, whether or not they received thyroid, also received vitamin E and/or diethylstilbestrol.

Twenty-one patients in this group were given thyroid. They included 11 of the 18 patients in the below normal range, 4 of whom had had a previous abortion. Thus, 7 patients in the below normal range and 11 of the patients who had had a previous abortion did not receive thyroid. The 18 patients in the above normal range did not receive specific therapy.

Ninety-seven (97) pregnancies terminated successfully. There were 3 neonatal deaths in Group I. The first was due to multiple congenital anomalies and occurred following cesarean section in a gravida ii, para ii, whose BMR was minus 21 per cent in the eighth week of gestation. This patient had been given thyroid. The second death was due to prematurity, occurring in a six months' fetus in a gravida iii with two previous abortions. The BMR was normal. This patient had been given thyroid as well as vitamin E and progesterone. The cause of the third death was not certain. It occurred following cesarean section in an overweight (202 pound, 65 inch) gravida iv, para ii, who had a normal BMR and who had not received thyroid.

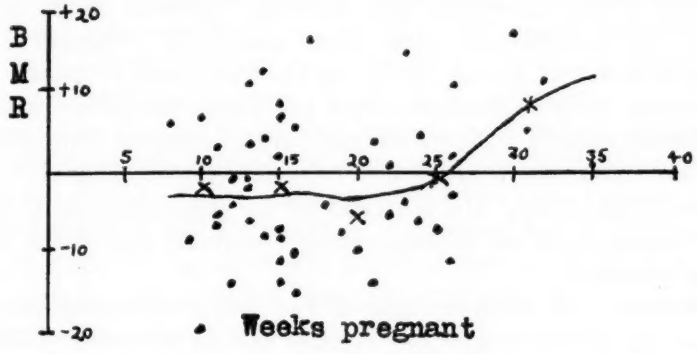

Fig. 3.

Group II.—The range and the average curve derived from the BMR determinations in Group II are shown in the scattergraph in Fig. 3. It is apparent that the average curve very closely approximates those in Figs. 1 and 2. Thirty-nine were in the normal range; 5 were more than 10 per cent above normal; and 6 were more than 10 per cent below normal. Two patients out of the 6 with BMR more than 10 per cent below normal did not receive thyroid; and the 5 patients with BMR more than 10 per cent above normal received no specific therapy.

Group II was divided into three classes: (1) BMR more than 5 per cent above average for the time in gestation during which the test was done—16 patients; (2) BMR more than 5 per cent below the average—11 patients; and (3) average BMR within plus 5 per cent to minus 5 per cent of average—19 patients. It should be noted that there is a difference in the total number of cases in some of the comparisons. This is because thyroid was given in four cases; one patient had twins; and the reliability of one patient's last menstrual period is in doubt. The results are summarized in Table II.

In regard to the length of gestation and the weight and sex of the infant, the data show no significant variation (in any of the three classes). Where

there is a substantial variation, as in the average maternal weight gain, the trend is not significant.

All pregnancies in Group II had a successful outcome.

TABLE II

	NORMAL		ABOVE 5%		LESS THAN -5%	
	RESULT	NO. OF PATIENTS	RESULT	NO. OF PATIENTS	RESULT	NO. OF PATIENTS
Average length of gestation*	281.3 days	19	280.8 days	15	274 days	11
Average gain in weight†	22.8 pounds	19	15.8 pounds	16	18.2 pounds	11
Average infant weight at birth‡	6.9 pounds	18	7.0 pounds	16	6.9 pounds	11
Sex of infant						
Male§	10		8		9	
Female	10	19	8	16	6	15

*5 cases excluded (4 received thyroid, 1 questionable last menstrual period).
†4 cases excluded (4 received thyroid).
‡5 cases excluded (4 received thyroid, 1 case twins).
§Includes twins, both boys.

Comment

The purpose of this paper has been to study the basal metabolic rate during pregnancy for correlations with other aspects of pregnancy, especially correlations which might prove useful in the care and/or prognosis of the case. The average curves obtained from the basal metabolic rates taken in this study coincide closely with an average curve derived from Javert's condensation of an extensive literature. This correlation, therefore, seems to validate the conclusions that the material of the present study is representative and that selection of the average basal metabolic rate for a given week of gestation is accurate.

The traditional and primary use of the basal metabolic rate in pregnancy has been to ascertain whether thyroid should be given, presumably to prevent spontaneous abortion. In the combined series of 150 patients, 24 had a BMR more than 10 per cent below the normal average for the time in pregnancy which the test was made. Fifteen of these patients received thyroid. (In one case, it was not started until the tenth lunar month.) All of the 24 patients had successful pregnancies. Although there is no way of knowing what might have happened if thyroid had not been given in the 15 treated cases, the basal metabolic rate was without useful significance whatsoever in at least 9, and most probably 10 cases. Preliminary work by Peters and associates[7] on the precipitable iodine in the serum casts further doubt on the usefulness of the basal metabolic rate during pregnancy as a guide to the use of thyroid to prevent spontaneous abortion. The precipitable serum iodine has been demonstrated to reflect accurately the activity of the thyroid gland and to be uninfluenced by extraneous factors. Peters showed in a small group of cases that in successful pregnancies the concentration of such iodine rises appreciably very shortly after the first missed period; whereas, when the rise in concentration of precipitable iodine fails to occur, abortion usually ensues.

After the rise of the precipitable iodine occurs, its level remains constant throughout the pregnancy. As Peters points out, the failure of the iodine level to parallel the basal metabolic rate changes is strong evidence that the rise of the basal metabolic rate in the last half of pregnancy cannot be ascribed to hyperplasia or increased activity of the thyroid gland as postulated by some authors and mentioned in the introduction here.

Since this failure of the precipitable iodine to rise may occur in women with normal BMR and normal iodine levels at the onset of pregnancy, and, since no correlation between the BMR and abortion has been demonstrated, the BMR obviously cannot be used routinely as an indication for the use of thyroid to prevent abortion in early pregnancy. This is not an argument against either the use of thyroid or the use of the BMR in sterility work. Their value is well known and Javert[8] in a recent study of 211 habitual aborters (three or more consecutive spontaneous abortions) at the Woman's Clinic of the New York Hospital found that 50 to 65 per cent had a low BMR (degree of abnormality was not given). The use of the test certainly is justified before pregnancies as part of the investigation of problem cases.

Summary and Conclusions

A single basal metabolic rate determination was taken at various intervals during the pregnancies of one group of 100 women and of another group of 50 women. Average curves were obtained in both groups and showed the BMR to be approximately minus 3 in the early weeks of gestation, rising after a small dip about the twenty-second week to approximately plus 10 per cent near term. This is essentially the same curve as obtained by a summary of the literature. Twenty-three patients had a BMR more than 10 per cent above and 24 patients had a BMR more than 10 per cent below the average BMR for the week of gestation in which the test was taken. Thyroid was given to 15 of the 24 patients with a BMR more than 10 per cent less than the average. All 24 patients had successful pregnancies.

No correlation was found between the BMR and: (1) history of previous spontaneous abortion; (2) incidence or outcome of threatened abortion; (3) the length of pregnancy; (4) the average weight gain of the mother; (5) the average weight of the offspring; and (6) the sex of the offspring.

This study, together with a report by Peters and co-workers to which reference is made in the comment, is taken to demonstrate that the routine use of the basal metabolic rate in pregnancy is of very doubtful value.

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A STUDY OF ONE HUNDRED FIFTY-THREE INFANTS PLACED IN THE POSITIVE PRESSURE OXYGEN-AIR LOCK

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THIS study was undertaken to evaluate the positive pressure oxygen-air lock as an instrument for resuscitation of the newborn infant. The only previous reports have been by Bloxsom,[1, 2] who designed the apparatus and apparently used the same principle as employed by Barach[3] to produce continuous immobilization of the lung in patients with pulmonary tuberculosis.

The positive pressure oxygen-air lock is a closed cylinder in which an infant can be placed and locked. The cylinder is made of transparent plastic so that the infant can be easily observed. Heat and humidity are provided in proper amounts. Air and oxygen are introduced under pressure, and a positive pressure is maintained. This positive pressure is cycled between one and three pounds at one-minute intervals. The pressure changes are automatically controlled by means of a mercury switch. A safety valve to control excessive pressure is provided.

The operation of this machine is relatively simple and an attendant can be taught how to operate it in a matter of a few minutes.

The mechanism of resuscitation is threefold. First, the constant positive pressure of at least 1 pound allows a pressure on the skin and pulmonary tree which forces oxygen by diffusion into the infant's circulation, thereby providing a high oxygen tension. The build-up phase also forces additional oxygen into the bronchial system. Second, the theory of expanding gases is employed, i.e., under decreasing pressure gas expands. The drop-off phase permits this expansion of gas due to the decreased pressure. Third, gaseous expansion causes a reverse flow in the bronchial system, and the expanding gas carries released carbon dioxide and fluid from the lungs.

Material

This study covered a period from May 23, 1951, through Jan. 12, 1952. During this time, there were 1,203 deliveries in the obstetrical department of the United States Army Hospital, Fort Benning, Ga. One hundred fifty-three infants were placed in the air lock.

Method

Infants of the following categories were placed in the air pressure lock (Table I):

I. Every infant delivered by cesarean section.

II. Premature infants. This included all available live fetuses regardless of their gestational age, size, or weight. Actually there were 96 prematures delivered during the period of this study, but only about one-half, 46 to be exact, were placed in the apparatus. This was principally due to the fact that the infants were not considered to be premature at time of birth, were good babies, and were found to be immatures only by weight.

III. All infants that appeared depressed and did not respond immediately to routine aspiration with soft-rubber bulb syringe and the use of moderate physical stimulation. Depression was considered to exist if the infant did not gasp or breathe within the first minute of life. This category included infants from pre-eclamptic mothers and heavily narcotized mothers. It also included prematures that were depressed and infants from the following three categories that were depressed. This category must of necessity represent much duplication of infants found in other categories.

IV. Infants with abnormal presentations.

V. Infants subjected to forceps rotations and difficult forceps deliveries.

VI. Infants from mothers who had extensive antepartum bleeding (over 500 c.c.) such as in placenta previa, abruptio, and ruptured marginal sinus.

VII. Infants from mothers who had prolonged labors with or without uterine inertia.

VIII. Infants from mothers with severe pre-eclampsia.

IX. Infants with severe hemolytic disease of the newborn.

Following a vaginal delivery, aspiration (by bulb syringe) was done on most of the infants before they were placed in the "lock." No aspiration was done on the cesarean section babies.

Once placed in the "lock," the infant was not disturbed until regular respirations had become established for at least thirty minutes. Any newborn requiring specific medication was removed for this. Some of the babies were returned to the lock because of labored respirations or cyanosis.

An analysis of each case was made during the immediate neonatal period. Notation was made of analgesia and anesthesia, type of delivery, maternal complications, time of first cry and respiration, onset of regular respiration, color of infant, etc.

Autopsies were performed on 85 per cent of the infants that died.

TABLE I. INDICATIONS FOR PLACING INFANTS IN POSITIVE PRESSURE OXYGEN-AIR LOCK

Infants delivered by cesarean section		21
Prematures (infants weighing 2,500 grams or less)		46
Under 1,000 grams	5	
1,000 grams and over	41	
Depressed (infants who did not breathe within one minute)		44
Abnormal presentations		58
Breech	48	
Persistent posteriors	8	
Arrested transverse	2	
Difficult forceps deliveries		10
Excessive antepartum bleeding (500 c.c. or more)		13
Placenta previa	6	
Abruptio placentae	6	
Ruptured marginal sinus	1	
Hemolytic disease of the newborn		5
Pre-eclampsia		8

Comment

All infants delivered by cesarean section were placed in the air lock without aspiration of the nose or mouth. This was done to evaluate Bloxsom's statement that the apparatus would cause "an outpouring of fluid and secretions from the mouth and nostrils." In 5 out of 21 infants this phenomenon was noted within a period of two to three minutes. None of the babies delivered by cesarean section died. We felt that we had caused these infants no harm by not aspirating them. We were able to confirm Bloxsom's report regarding the expression of fluids.

Babies born in the previable period (Table II) were placed in the air lock principally to see how small an infant could be kept alive and for how long a time. Observations indicated that the nonbreathing newborn was being helped by the "lock," for, despite extremely irregular respirations, these immatures lived for considerable periods of time. Of extreme import was that they also appeared well oxygenated. This confirmed the observations made by Eastman[4] in a group of "abortuses." We felt that the positive pressure was helpful in forcing more oxygen into the circulating blood where respiration is incompletely established.

Other prematures added additional evidence. Frequently, when removed from the air lock after respirations were stabilized, they would become cyanotic or have respiratory difficulty and would often have to be returned to the "lock."

The "depressed" infant interested us especially, for we felt that here, as well as in the premature, the apparatus was actually lifesaving for an occasional newborn. In the heavily narcotized baby the "lock" played one of its most important roles since it appeared that such infants could be oxygenated even if they did not breathe for several minutes. As important as the oxygenation was the fact that this was accomplished without trauma to the infant.

TABLE II. INFANTS UNDER 1,000 GRAMS THAT WERE OBSERVED IN THE AIR LOCK

CASE NO.	GESTATIONAL AGE IN WEEKS	WEIGHT IN GRAMS	LIFE SPAN IN HOURS
1	22	368	2
2	24	567	3
3	25	907	1
*4	26	694	5
*5	26	722	8

*Twins.

Fig. 1 shows the time interval between delivery and first respiration of all infants placed in the air lock, exclusive of newborns under 1,000 grams. Fifty-five babies breathed in the first thirty seconds; 104 within the first minute.

Of the 44 infants in the "depressed" group, 22 breathed in the second minute after birth. We felt that they would have done well with the other standard forms of resuscitation.

Twenty-two required more than two minutes to take the first respiration (Table III). Fourteen took from three to five minutes to breathe. We felt that the Bloxsom air lock was one of the best methods of treatment yet devised for the management of this group. It was quite impressive to observe that within a few seconds after being placed in the lock many of these babies began to appear oxygenated.

Eight of the depressed infants took more than five minutes to take their first respiration. Seven of these infants are alive and well; one died of brain hemorrhage. It was our opinion that one or more of these infants would have died had the apparatus not been used.

Excessive ante- or intrapartum bleeding definitely contributed to the depression of the infant. A review of Table III reveals a number of these cases among the moderately or severely depressed infants. Almost 50 per cent of the mothers with significant bleeding (500 c.c. or more) had depressed infants.

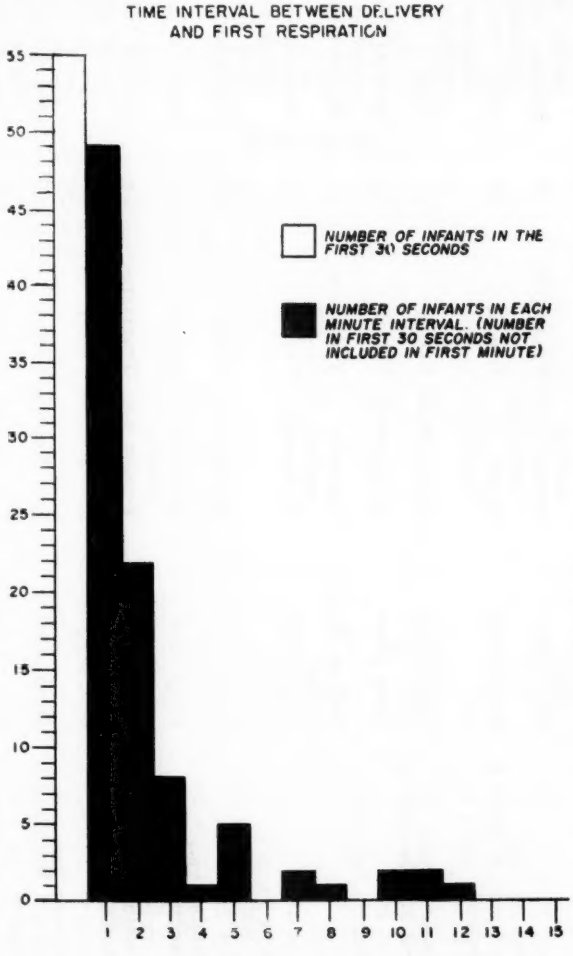

Fig. 1.

Out of 1,200 deliveries a salvage of one or 2 infants would affect the infant mortality rate only 0.1 to 0.2 per cent. The comparison of the total infant mortality rate for one year using the apparatus against the results obtained in one year without it would not show a significant improvement. However, if a comparison is made regarding only the infants demonstrating depression or trauma at birth, in this series 22 infants, an increased salvage of one or two infants becomes a significant improvement.

The place for the air lock is in the delivery room. When a cesarean section is being done, its place is in the operating room. It should be available to the obstetrician immediately upon the delivery of the child. The apparatus

TABLE III. PERTINENT INFORMATION ON 22 DEPRESSED INFANTS THAT REQUIRED THREE MINUTES OR LONGER FOR FIRST RESPIRATION

CASE NO.	RESP. TIME (MINUTES)	WEIGHT (GRAMS)	ANALGESIA AND AMOUNT*	TYPE OF ANESTHESIA	METHOD OF DELIVERY	PRESENTATION	GESTATIONAL AGE IN WEEKS	COMPLICATIONS AND REMARKS
1	3	3,402	Demerol 250 Scopolamine 1/150 × 2	Drop ether	Low forceps	Vertex	39	None
2	3	3,543	Demerol 400 Scopolamine 1/150 × 4	Pudendal block	Low forceps	Vertex	40	Persistent occiput posterior
3	3	2,622	Demerol 100 Scopolamine 1/150	Drop ether and local	Midforceps	Vertex	36	Severe vaginal bleeding due to abruptio with fetal distress
4	3	2,891	Demerol 200 Scopolamine 1/150	Drop ether and local	Midforceps	Vertex	37	Arrested transverse with forceps rotation
5	3	2,438	None	Sodium Pentothal	Cesarean section	Transverse	38	Severe vaginal bleeding, placenta previa, fetal distress
6	3	2,098	Demerol 100 Scopolamine 1/150	Drop ether	Version and extraction	Transverse	39	Second twin with prolapsed arm, prematurity
7	3	2,353	Demerol 400, Seconal 6 Scopolamine 1/150 × 4	Drop ether	Breech extraction	Breech	38	First twin, premature. Died, intracranial hemorrhage at post mortem
8	3	3,175	Scopolamine 1/150 × 2 Demerol 200, Seconal 3	Drop ether	Spontaneous	Vertex	40	None
9	4	5,167	Demerol 200 Scopolamine 1/150 × 2	Drop ether	Spontaneous	Vertex	42	Manual rotation, persistent posterior, large infant
10	5	2,493	None	Sodium Pentothal	Cesarean section	Transverse	35	Placenta previa, prematurity
11	5	2,126	Demerol 400 Morphine 1/4 × 2	Drop ether	Midforceps	Vertex	35	Forceps rotation, left occipitotransverse. Pre-eclampsia. Pitocin induced
12	5	2,438	Demerol 200 Scopolamine 1/150 × 2	Local	Spontaneous	Vertex	38	Prematurity
13	5	4,274	Scopolamine 1/150 × 2	Drop ether	Assisted breech	Breech	40	Large infant
14	5	2,140	Scopolamine 1/200 Scopolamine 1/150 × 2	Drop ether	Version and extraction	Transverse	40	Second twin, uterine inertia, prematurity
15	7	3,175	Nembutal 3 Scopolamine 1/200	Gas, oxygen, ether	Low forceps	Vertex	40	Inlet dystocia
16	7	4,451	Demerol 400, Morphine 1/4 Scopolamine 1/150 × 4	Drop ether	Low forceps	Vertex	41	Persistent occiput posterior, large infant
17	8	2,466	Demerol 100, Morphine 1/4 Scopolamine 1/150 × 2	Pudendal block	Low forceps	Vertex	38	Pre-eclampsia, prematurity
18	10	2,268	None	Drop ether	Low forceps	Face	37	Abruptio placentae, prematurity
19	10	3,543	Demerol 200 Scopolamine 1/150 × 2	Drop ether	Low forceps	Vertex	40	Severe vaginal bleeding due to ruptured marginal sinus
20	11	2,806	Scopolamine 1/150 × 2	Drop ether	Midforceps	Vertex	38	Uterine inertia, second stage 4 hours
21	11	3,005	Scopolamine 1/200 Morphine 1/6	None	Spontaneous	Vertex	41	Inactive, morphine given for rest. Sudden precipitate labor
22	12	3,402	Demerol 300 Scopolamine 1/150	Local block	Spontaneous	Vertex	40	Pre-eclampsia, died. Intracranial hemorrhage at post mortem

*Demerol is reported in milligrams. Morphine, Scopolamine, Seconal, and Nembutal are in grains. The local infiltrations and pudendal

is not designed as an incubator; it is an instrument for oxygenating the newborn infant during the period of greatest oxygen need, the apnea immediately after birth.

Conclusions

1. The study indicated that the positive pressure oxygen-air lock devised by Bloxsom could be used as a most valuable adjunct in the resuscitation of the newborn infant.

2. The air lock seemed to be lifesaving for the occasional depressed and/or premature infant.

We are grateful for suggestions from Dr. J. R. McCain. The Bloxsom apparatus was given to this hospital by the Fort Benning Chapter of The Daughters of the United States Army.

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*Demerol is reported in milligrams. Morphine, Scopolamine, Seconal, and Nembutal are in grains. The local infiltrations and pudendal hemorrhage at post mortem
Scopolamine 1/150

AN OPERATION FOR POSTOPERATIVE VESICOVAGINAL FISTULA*

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THE handling of vesicovaginal fistulas has gone through quite a transition since Marion Sims successfully operated on one vaginally in 1849, over 100 years ago. Innumerable operations have since been described for this condition —some by the vaginal, others by the vesical or transperitoneal route. None of these has really proved to be satisfactory. In cases where the vagina is not important, a partial colpocleisis was suggested and done by Latzko, Falk and Holden. They really created an artificial diverticulum of the bladder through the fistula's opening.

It is universally true that vesicovaginal fistulas may and very often do require more than one operation before success is attained. It is not unusual for a patient to have had three or four operations attempted. We have had under our care a patient who had thirteen operations for a vesicovaginal fistula without success. She eventually had the ureters transplanted into the bowel. Because of these failures, many gadgets have been invented to alleviate the inconvenience.

Counseller, at the Mayo Clinic, got 85 per cent cures in 181 cases. Ninety-eight patients had one to ten attempts elsewhere, and 61 patients had two to six attempts at the Mayo Clinic. Norman Miller reported 82 per cent cures in a similar series. There are good historical reviews of this subject by Howard Kelly in 1912 and by Norman Miller in 1935.

Most of the fistulas described were due to obstetric causes, such as a forceps or instrumental delivery that resulted in a laceration into the bladder, or a hard long second stage that produced ischemia and pressure necrosis which caused a hole in the bladder.

Today we see various other types. The greatest number now (about two-thirds) follow pelvic surgery. The increasing popularity of vaginal hysterectomies, total hysterectomies, and Wertheim operations has resulted in a greater incidence of vesicovaginal fistulas. Usually an area is caught by a suture and becomes devitalized. This is followed by ischemia and sloughing. Necrosis may also be produced by long indwelling pessaries, gummas, invasion by carcinoma, or following x-ray and radium therapy.

Obviously, in the group of fistulas that follow gynecological operations, the location of the fistula is much higher. Our problem is the one that follows these operations. The fistulas that open close to the vaginal outlet are best treated by the vaginal approach which is still the most convenient and usually gives good results.

*Presented at the Annual Meeting of the Society of Obstetricians and Gynecologists of Canada at Digby, Nova Scotia, June 23 to 25, 1950.

The problem arises when one encounters fistulas on the floor of the bladder and in the area of the trigone. Here the support and fixation that were present with the cervix in place are missing. It was for these obvious reasons that we considered a suprapubic extraperitoneal approach.

The symptoms of this type of fistula are simple. Following the operation, cystitis develops and is followed by incontinence in a few days. The vagina becomes irritated. Diagnosis is also easy. Methylene blue injected into the bladder will demonstrate the opening and differentiate a vesicovaginal from a ureterovaginal fistula. Cystoscopic examination is essential.

The principles of the repair are:

1. Good exposure and denudation of the fistula.
2. Extensive separation of bladder from vagina.
3. Inversion of the fistula.
4. Coaptation of raw surfaces without tension.

Preparation for this operation is made as for any other approach. After an accurate diagnosis has been made, including cystoscopic examination and ureteral catheterization, the kidney function determined, and the presence of ureteral strictures eliminated, the vagina and bladder are cleansed with vaginal douches. Antibiotics are administered. This regime is maintained until the bladder and vagina are clean. It may take four to eight weeks.

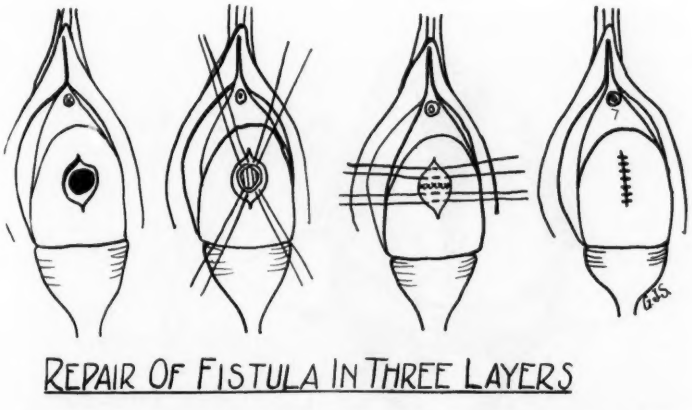

Fig. 1.—Vaginal approach for repair of vesicovaginal fistula.

Immediately prior to operation, ureteral catheters are inserted and the vagina is tightly packed with gauze, soaked in sulfathiazole emulsion. The patient is then given a spinal anesthetic and placed in a modified Trendelenburg position. A median suprapubic incision is made from the symphysis to the umbilicus, the fascia is incised, and the muscles are separated, exposing the vault of the bladder. The urachus is identified, clamped, and cut. Working extraperitoneally, the bladder is freed laterally and posteriorly to the scarred area which surrounds the fistulous tract. Here the peritoneum is involved and cannot be separated. So the peritoneal cavity is opened and the bladder freed

further. When loose and free, the peritoneum is closed. Now the bladder is separated from the vagina and we have one opening into the bladder and another into the vagina.

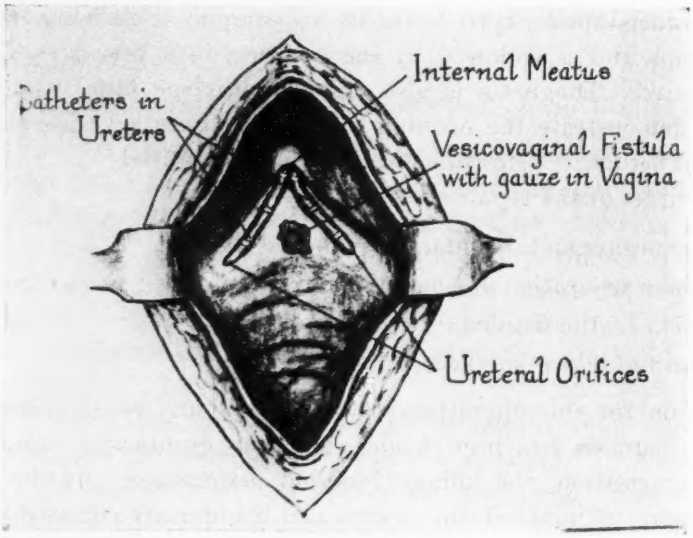

Fig. 2.—Abdominal approach to vesicovaginal fistula. View of interior of bladder showing location of fistula.

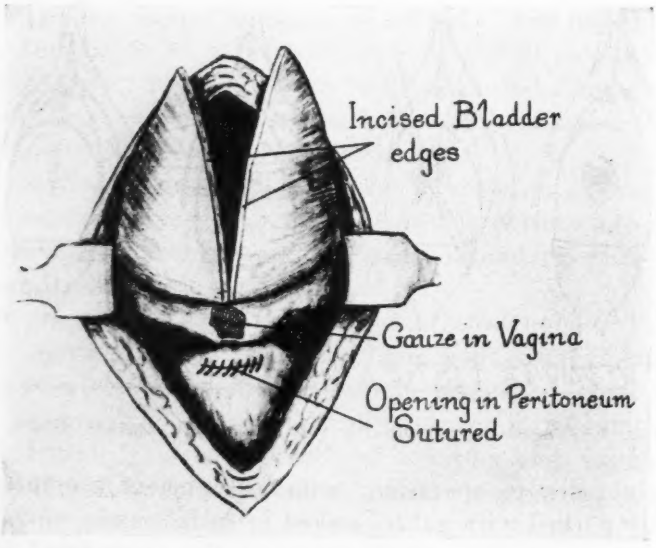

Fig. 3.—Scars from peritoneum to bladder have been resected. Peritoneum has been freed and then sutured.

The bladder is now opened at the vault and this opening is carried down to the site of the fistula where the scars of the bladder and vagina are excised separately. The opening into the vagina is closed transversely with No. 1 chromic catgut interrupted sutures in two rows crossing one another. Then the bladder is closed, beginning at the bottom of the new opening and working up to the

vault, with chromic catgut No. 1 for the bladder wall. The mucosa is allowed to invert. A Pezzer catheter is inserted and sutured into the final small openings in the dome of the bladder. Two drains are inserted. One goes down to the suture line and the other into the prevesical space. The wound is closed in layers with interrupted sutures.

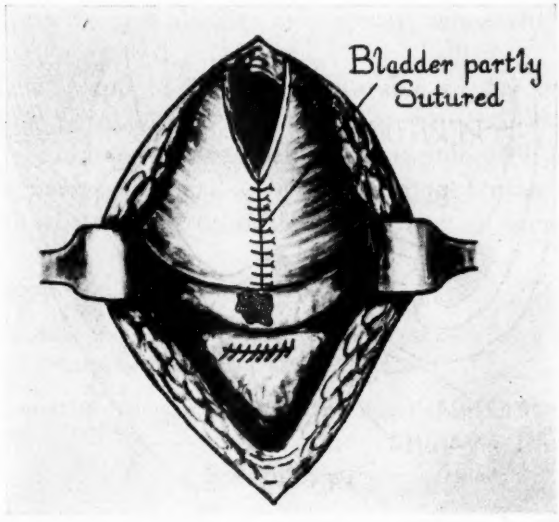

Fig. 4.—Same as Fig. 3 but part of bladder wall has been sutured. Bladder mucosa is allowed to invert.

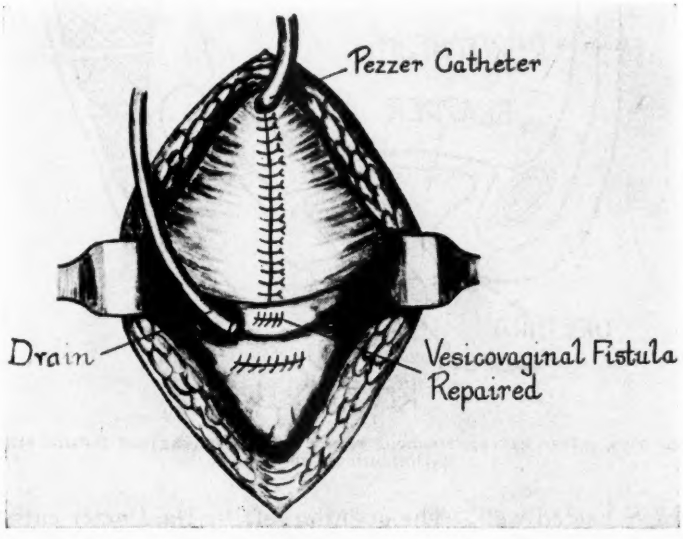

Fig. 5.—Fistulous opening into vagina has been resected and sutured. Bladder wall has been sutured up to small opening in dome of bladder where Pezzer catheter is inserted. One drain is in place.

In one case it was necessary to open the bladder prior to its separation from the peritoneum due to the presence of a marked pericystitis with adhesions of the peritoneum to the bladder.

The Pezzer catheter is retained in the bladder for two weeks and then removed, and a transurethral self-retaining catheter (Foley) inserted and left in for about three weeks more. This catheter is changed every five or six days and a new one inserted. We do not recommend irrigation of the Pezzer or self-retaining catheter unless blockage occurs. It must then be done with the utmost precaution. Antibiotics are given for eight to ten days, and in all cases

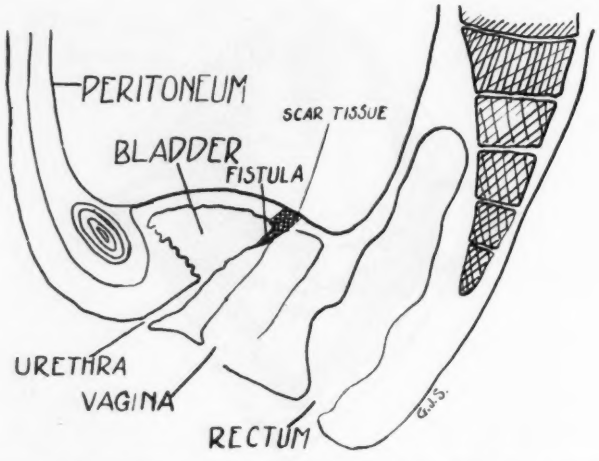

Fig. 6.—Sagittal view of anatomic relationship of fistula to bladder, vagina, and peritoneum. Uterus had been removed at previous operation.

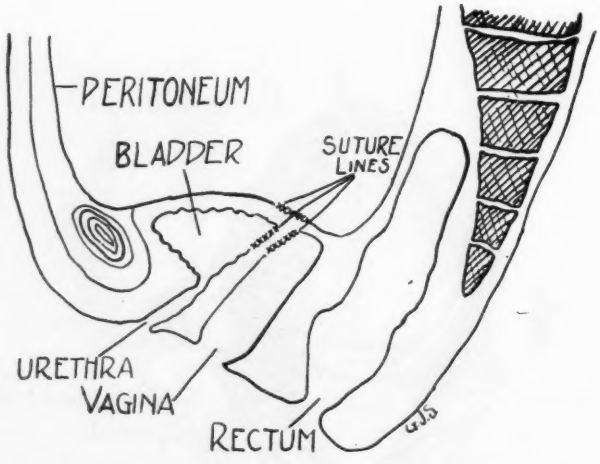

Fig. 7.—Sagittal view after extraperitoneal repair for vesicovaginal fistula showing similar relationship as in Fig. 6.

the wounds have healed well. The opening left by the Pezzer catheter has closed spontaneously in seven to ten days. The patients have all been perfectly continent at the end of six weeks and have remained so. We have now operated upon three patients who have responded very well to this operation, none requiring a second attempt. The fistulas in this group followed gynecological operations and for different reasons could not be handled well from below.

In summarizing I would like to emphasize a number of points:

1. The long preoperative preparation so as to eliminate the inflammation in the bladder and the vagina.

2. Insertion of ureteral catheters at the time of operation to act as guides so as to avoid injury to the ureters.

3. Tight packing of the vagina with gauze just before operation so as to prevent further injury to the bladder and rectum when the bladder is being separated and the fistula excised.

4. The midline suprapubic incision, preferable to the transverse because we feel it gives us a better exposure.

5. Prolonged continuous drainage, first suprapubically and then transurethrally for at least five weeks, to allow healing without tension.

6. No irrigation of drainage tubes unless obstruction occurs and then only very carefully.

7. Pre- and postoperative antibiotic therapy.

Addendum.—Since this paper was read, two more patients have been operated upon for similar vesicovaginal fistulas with very satisfactory results.

This work was done with the cooperation of Dr. Max Ratner and Dr. M. Siminovitch of the Urology Department.

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AN INCISION TO FACILITATE RADICAL PELVIC SURGERY IN WOMEN

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WHEN Pfannenstiel[1] described the incision which bears his name he prescribed certain limitations to its use. He felt that cases in which rapid entrance into the peritoneal cavity was imperative, such as in ruptured ectopic pregnancy with severe intraperitoneal hemorrhage, should be operated upon through some other type of incision. Likewise, cases of large tumors or cysts were not suitable because insufficient working space was provided by the incision.

In cases of carcinoma of the rectum in which an abdominoperineal resection is performed, the midline or left rectus incision has not been found satisfactory for the colostomy opening because of the marked eventration of the abdominal wall which results. Consequently, the terminal sigmoid is best brought out through a separate muscle-splitting incision in the left lower abdominal quadrant similar to a McBurney incision on the right.

In cases where exposure of the hypogastric and iliac vessels is necessary as in the Taussig[2, 3] operation of lymphadenectomy the procedure must be carried out transperitoneally, if a lower midline incision is performed, unless separate incisions are made in each groin. If ligation of the hypogastric arteries is anticipated as a part of or preliminary to the operation, the extraperitoneal approach facilitates the procedure remarkably.

The limitation of rapid entrance into the peritoneal cavity prescribed by Pfannenstiel is applicable to the incision about to be described, but the limitation of operative space is not applicable, because adequate space is provided for all but the huge pelvic cysts and tumors. In addition, it provides exposure of the iliac and hypogastric vessels and associated lymph glands; permits early identification of the ureter and the uterine vessels; and it provides the ease and security of closure afforded by the Pfannenstiel incision. By early ligation of the deep epigastric vessels the fascial layer can be rapidly stripped upward from the rectus muscles with insignificant bleeding. The rectus muscles are not transected.

Technique

The incision is begun about one inch medial to the anterior superior iliac spine and is carried caudad parallel to Poupart's ligament toward the symphysis pubis. It crosses the midline about one inch above the symphysis pubis and is continued upward on the other side of the lower abdomen to complete the other limb of the U, parallel to Poupart's ligament and terminating about one

inch medial to the opposite anterior superior iliac spine. This original U-shaped incision is carried right down to the fascia of the anterior rectus sheath and the external oblique aponeuroses. The skin may be scratched in several places preliminary to the incision to facilitate an accurate skin approximation during closure of the wound. The fascia is cleared for a distance of about one inch cephalad and caudad to permit easier approximation of the fascia during closure. All superficial vessels are caught with hemostats and ligated. Following the original line of the skin incision, the anterior sheaths of the rectus muscles, the external, and internal oblique muscles, and aponeuroses are incised and the minor bleeding secured with suture ligatures. At this point in the incision, the deep epigastric vessels are easily identifiable as they enter the rectus sheath obliquely from below. They are clamped, cut, and ligated. The anterior rectus sheath can then be stripped up to the umbilicus without difficulty and with almost no bleeding. It is grasped on each side of the midline with forceps. Traction is applied upward and it is dissected free in the midline, linea alba, from the underlying peritoneum.

The peritoneum is now reflected back from the iliac vessels, if ligation of the hypogastric arteries or lymphadenectomy is to be performed. The hypogastric arteries are best exposed by placing a pack medial and cephalad and retracting in the same direction. The artery is slightly more difficult to expose on the right than the left. If the operator stands on the side opposite to the hypogastric artery he is exposing, the procedure is facilitated. The uterine arteries can also be seen clearly turning medially into the parametrial areas. They may also be ligated if desired, flush with the lateral pelvic wall. The rectus muscles are separated in the midline and the peritoneum incised longitudinally to as great a length as the exposure permits.

When the intraperitoneal procedures have been completed, the peritoneum is closed in the midline, the rectus muscles are tacked together with interrupted stitches of plain catgut. The fascial incision is closed with chromic catgut, care being observed to secure both layers of fascia lateral to the rectus sheaths. The skin is then closed as desired.

If resection of the rectum has been performed, the colostomy is done by puncturing a hole in the peritoneum to the left of the left rectus muscle and bringing the terminal sigmoid through this aperture. Closure is then performed as previously except for the placing of fascial sutures. A chromic catgut stitch is started on each side of the colostomy and carried to the termination of the incision on the respective side. Thus two continuous chromic catgut stitches are inserted instead of one.

Illustrative Cases

CASE 1.—Mrs. E. M., a white woman aged 68 years, was admitted to the hospital Nov. 28, 1950, bleeding from the rectum, and with a protrusion from the vagina.

Essential findings were: Red blood count 2.89 million, Wassermann test negative, blood pressure 154/80, nonprotein nitrogen 35.7, and blood sugar 123.

Diagnosis: Carcinoma of the rectum about 2 inches above the anal orifice, complete prolapse of the uterus.

Three blood transfusions were given prior to surgery.

Surgery: On Dec. 1, 1950, an incision was made as described above, with extraperitoneal ligation of the hypogastric arteries. Abdominoperineal resection of the rectum, and total hysterectomy, with bilateral salpingo-oophorectomy were performed. Terminal sigmoid colostomy was brought out to the left of the left rectus muscle. The perineal portion of the resection was performed with the patient in the lithotomy position. The dissection was started by elevating and longitudinally incising the mucosa of the posterior vaginal wall. After the cul-de-sac was entered, the ligated stump of the terminal bowel was brought out through the

incision. The skin about the anus was then incised and the terminal bowel was removed by cutting the levator ani muscles. The sphincter muscles were removed with the specimen. The defect was then closed by continuous suture of the cut ends of the levator ani muscles. A Penrose drain was inserted in the cul-de-sac beneath the mucosa of the posterior vaginal wall. The perineum was closed tightly as in a posterior colporrhaphy.

Preliminary ligation of the hypogastric arteries made the hysterectomy and the perineal excision almost bloodless. Healing was rapid and uneventful. She was discharged from the hospital on Dec. 12, 1950.

Summary of Surgical Pathological Report: "Retrogressed hyperplasia of the endometrium. Subinvolution of the uterus. Hypertrophied cervix. Chronic endocervicitis with erosion. Adenomatous cervical polyp. Bilateral pathologically negative Fallopian tubes. Bilateral cortical cystomata of ovaries. Multiple corpora albicantia of ovaries. Resection of rectosigmoid. Ulcerating penetration carcinoma of the rectum. Hyperp'asia of mesenteric lymph nodes."

Fig. 1.

CASE 2.—Mrs. A. B. was a white woman, aged 77 years (Fig. 1). Her chief complaint on Jan. 11, 1952, was bleeding from the vaginal tract for the past year. Vaginal examination disclosed a uterus enlarged to the size of a 4 to 5 months' pregnancy with bloody discharge exuding from the cervix. She was admitted to the hospital on Jan. 14, 1952.

Surgery: On Jan. 15, 1952, an incision as described above was employed. Bilateral ligation of the hypogastric arteries was performed and the uterine arteries were ligated near the lateral pelvic walls. Bilateral salpingo-oophorectomy, total hysterectomy, and excision of the upper portion of the vagina were performed.

Recovery was uneventful. The patient was discharged from the hospital in good condition on Jan. 23, 1952. Postoperative x-ray therapy was carried out in this case.

Summary of Surgical Pathological Report: "Microscopic examination: The specimen was a uterus measuring 12.5 by 9.5 by 7.5 cm. The specimen had been partially opened to reveal a large pinkish-white tumor filling the endometrial cavity and destroying the myo-

metrium. In the upper part of the specimen the tumor was polypoid, firm, and grayish white. The lower portion of the uterus showed a polypoid tumor growth with erosion and destruction of the uterine wall. The polypoid changes extended down to involve the isthmus but did not extend to the portio of the cervix. On section the polypoid areas were somewhat soft and friable while the upper portion showed firm grayish-white tumor tissue, which appeared partially circumscribed. Sections of the polypoid areas described above showed a tumor made up of well-formed glands, which were lined by anaplastic epithelium.

"There were many mitotic figures and the glands produced were abnormal and bizarre in shape and size. Sections of the more solid portions described above showed considerably more stroma and in these areas there were also malignant cells. There was suggestion of bundle arrangement remaining in several areas and the cells present in these zones were very irregular in size and shape with many large giant forms visible. The changes in this area would suggest a tumor arising from a smooth-muscle tumor. Thus the microscopic findings suggested that two tumors were existent in this uterus, namely, an adenocarcinoma arising in the endometrial cavity together with a leiomyosarcoma originating in a previous leiomyoma.

"Diagnosis: 1. Adenocarcinoma of the endometrium. 2. Leiomyosarcoma."

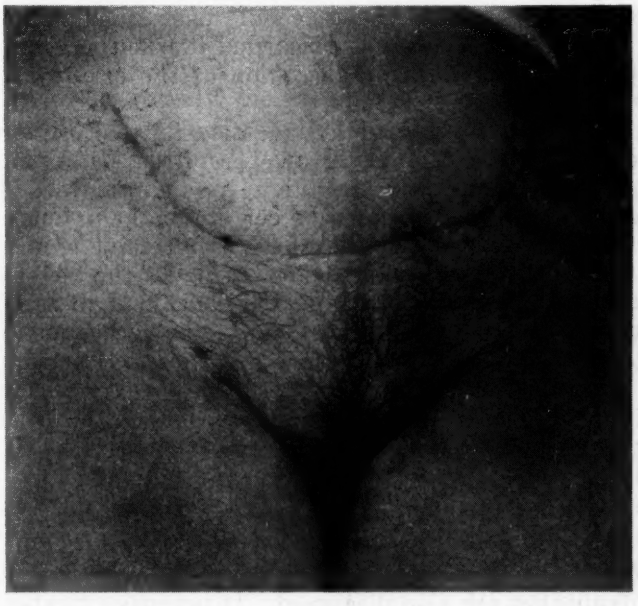

Fig. 2.

CASE 3.—Mrs. E. H. was 67 years of age (Fig. 2). Her chief complaint on Feb. 22, 1952, was swelling of the abdomen. Her pulse was 88, blood pressure 194/94. Abdominal examination disclosed a tumor mass extending above the umbilicus. Vaginal examination disclosed a cystocele and polypoid tumor projecting from the cervix. Kahn and Kline tests were negative, blood sugar was 100 mg., nonprotein nitrogen 33.1 mg. per 100 c.c. Chest x-ray was negative. She was admitted to the hospital on March 21, 1952.

Surgery: On March 24, 1952, an incision was made as described above with bilateral ligation of the hypogastric arteries and the uterine arteries near the pelvic wall. A huge cyst of the left ovary was found adherent to the sigmoid. No difficulty was encountered in delivering the cyst once it was freed. Bilateral salpingo-oophorectomy and a total hysterectomy were performed. The patient was discharged on May 1, 1952, in good condition. Recovery was uneventful.

Summary of Surgical Pathological Report: "The left ovary was transformed into a cystic mass measuring 18 by 18 by 5 cm. A Fallopian tube was attached 6 cm. long and 0.5 cm. in circumference. The surface of the cyst was smooth. Contents were an excessive

amount of an inspissated hemorrhagic matter, which was adherent to the inner wall of the cyst. The cyst wall measured in areas up to 1.5 cm., in other areas the wall was tissue-paper thin. The thickened area was yellow in color and may have represented remnants of the original ovary. In some places where the previously described blood was attached, the wall apparently had undergone infarction. There was no evidence of papillary structures lining the inner wall of the cyst.

"*Microscopic Diagnosis:* Atrophic (senile) endometrium. Subinvolution of the uterus. Hypertrophied cervix. Marked glandular cervical hyperplasia with formation of numerous Nabothian cysts. Papillary endocervicitis with erosion. Chronic cervicitis. Inflamed fibroglandular cervical polyp. Unilateral healed interstitial salpingitis. Contralateral pathologically negative Fallopian tube. Unilateral chronic adhesive perioophoritis. Serous cystadenomas of bilateral ovary (partly cortical)."

The recent enthusiasm regarding the Wertheim operation for carcinoma of the cervix has also revived interest in the ligation of the hypogastric arteries as a means of reducing and controlling bleeding. Ligation of these vessels is greatly facilitated by the incision described above. Wertheim[4] utilized the procedure in the performance of his radical hysterectomy in his thirteenth to twenty-first cases, but discarded it when he found that bleeding was not completely controlled in the region of the cervix as a result of the ligations.

Hartman and Quenu[5] utilized hypogastric ligations in their abdominal-perineal resections of the rectum. However, after Miles[6] modified the procedure, that part of the operative technique was eliminated. In the performance of hypogastric ligation one must be certain of the patency of the external iliac vessels to avoid gangrene of the foot. Progressive enlargement of metastatic glands or encroachment of tumor tissue on the external iliac vessels may completely obliterate them and permit the blood to reach the lower extremity through the hypogastric vessels. If the hypogastric artery is now ligated the blood supply to the lower extremity is severely compromised. This complication developed in one of my first cases where carcinomatous tissue had occluded the external iliac vessels. Ligation of the hypogastric vessels in this case produced gangrene of the distal portion of the foot on the corresponding side.

Summary

An incision is described which facilitates radical pelvic surgery. Its limitations and advantages are also discussed. It permits extraperitoneal ligation of the hypogastric and uterine arteries. It also facilitates lymphadenectomy as described by Taussig. Patency of the external iliac vessels should be verified before the hypogastric artery is ligated.

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ENDOMETRIOSIS OF THE CERVIX UTERI*

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THERE are only twelve reported instances of cervical endometriosis in the literature (Fels,[1] Rushmore,[2] Fobe,[3] Henriques,[4] Hobbs and Lazar,[5] Lash and Rappaport,[6] Siddall and Mack,[7] and Navrath[8]). It is considered to be a rare condition. We doubt, however, that this is true since we have observed sixteen such lesions and all but one during the last four years.

The infrequency of reported instances of cervical endometriosis may result from lack of observation of the gross lesion because it is often quite small. Second, diagnosis depends on cervical biopsy. Many clinicians do not have cervical biopsy forceps readily available in the office and do not biopsy all abnormal-appearing areas; in other words, they are not "biopsy conscious." Many are also hesitant to do biopsies because of the laboratory fee charged to the patient. Third, since these lesions are often small, biopsies must be accurately taken without causing trauma or crushing of the tissue; otherwise, microscopic confirmation of endometriosis may be difficult. The microscopic preparations must, therefore, be of the best quality and the individual interpreting the slides must be "endometriosis conscious."

Material

The sixteen instances of cervical endometriosis reported here were from patients seen by the first author and from the files of the laboratory of the Department of Obstetrics and Gynecology of Northwestern University Medical School. None has been previously reported. All were located on the pars vaginalis of the cervix. Specimens from three patients were not included because the lesions were found only in the endocervix. Specimens from two other patients were not included because only endometrial stroma was observed; despite multiple sections, no endometrial glands were found. All sixteen instances herein reported may be considered "primary endometriosis of the cervix" as discussed by Lash and Rappaport. This means that the reported lesions were limited to the cervix and were not extensions of endometriosis from the rectovaginal septum or from the serosal surface of the supravaginal portion of the cervix.

In eight of our patients the cervical endometriosis produced no symptoms. The symptoms that did occur were similar to those of early cervical carcinoma, i.e., intermenstrual (usually premenstrual) spotting or brownish discharge (6 cases), postcoital bleeding (1 case), or both of these symptoms (1 case).

Table I lists the gross descriptions of the endometrial lesions of the cervix as they were recorded by the various clinicians. Although the lesions were not

*Presented before the Chicago Gynecological Society, Jan. 18, 1952.

described in detail, there were apparent variations in the gross appearance. These variations may result from different phases of the menstrual cycle producing differing physiologic responses in the endometriotic lesion, or from different duration and/or extent of the lesion. Six lesions were described as red, mottled areas or red, elevated, velvety areas. Two lesions appeared as small bluish nodules 2 mm. and 5 mm. in diameter, respectively; while another was described as a 2 mm. blue "blood blister." Another lesion was a 2 mm. superficial ulcer on the cervix. In one patient endometriosis was found in "friable areas on the cervix." In two patients carcinoma of the cervix was suspected although one lesion was described as a papillomatous growth and the other as a red mulberry lesion. In three patients no specific lesions of the cervix were described. However, the endometriosis was discovered microscopically in the removed tissue.

TABLE I. GROSS DESCRIPTIONS OF LESIONS ON THE CERVIX

Slightly elevated, red, velvety lesion	4
Small red circumscribed area	1
Papillary lesion on cervix (grossly like carcinoma)	1
Red mulberry lesion (grossly like carcinoma)	1
2 mm. superficial ulcer on cervix	1
2 mm. blue "blood blister"	1
Bluish nodule (2 mm. and 5 mm., respectively)	2
Few small red mottled areas	1
Friable areas on the cervix	1
No specific lesions	3
	16

Table II records the previous gynecologic operations on the sixteen patients; thirteen had had operations and twelve of the thirteen had had procedures which caused direct trauma to the cervix. Therefore, in seems that cervical endometriosis may result from mechanical transplantation of bits of endometrium into tenaculum holes, or into the squamous epithelium of the pars vaginalis of the cervix which has been traumatized during an operation.

TABLE II. HISTORY OF PREVIOUS GYNECOLOGIC OPERATIVE PROCEDURES

Dilatation and curettage	7
Cervical amputation	4
Supracervical hysterectomy	1
Cervical repair on fourth postpartum day	1
None	3*
	16

*All were multiparas.

The remaining three, who gave no history of gynecologic surgery, were multiparas. It is possible that bits of endometrium were implanted into cervical lacerations during, or soon after delivery. This assumption is supported by the fact that implantation endometriosis is found on rare occasions in episiotomy scars.

The brief history of one case is noteworthy:

Mrs. R. F., a 25-year-old nulliparous white woman, complained of dysmenorrhea ever since the menarche. She was seen by the first author on Feb. 17, 1949. Except for stenosis and acute anterior angulation of the cervix, the genital organs were normal. On Feb. 21, 1949, the cervix was widely dilated; endometrium obtained by curettement was in the proliferative phase. Menstruation was painless until September. On Sept. 13, 1949, a 2 to 3 mm. red, elevated, velvety, lesion was noted 4 mm. directly above the external os of the cervix.

Fig. 1.

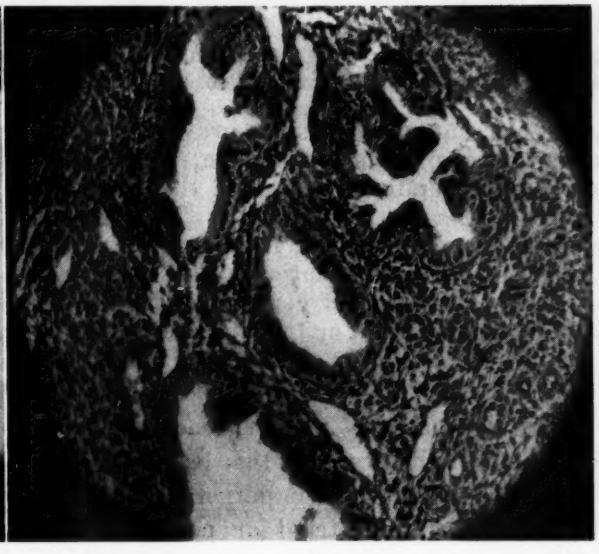

Fig. 2.

Fig. 1.—Endometriosis of the cervix immediately beneath the squamous epithelium. A tracheloplasty had been done three years prior to biopsy.

Fig. 2.—High power of Fig. 1 showing typical midsecretory endometrium.

Fig. 3.

Fig. 4.

Fig. 3.—Endometriosis beneath the squamous epithelium of the pars vaginalis (this patient had a cervical amputation four years prior to biopsy).

Fig. 4.—High power of endometriosis from same case portrayed in Fig. 3. Note that glands are in the proliferative phase.

Biopsy revealed endometrial glands and stroma in cervical tissue. One surface was covered with squamous epithelium. At one very narrow point an endometrial gland seemed to have grown through the squamous epithelium. (This may have been the original point of perforation produced by a tenaculum on Feb. 21, 1949.)

Optimum conditions for growth of transplanted endometrium include (1) a sterile recipient site (Markee[9]), and (2) a moderately high estrogen blood level corresponding to that of the late proliferative phase of the menstrual cycle (Hobbs and Bortnick[10]). The vagina is never sterile and an optimum blood estrogen level for implantation and growth of endometrium in a new site is not of long duration. These factors probably explain why we do not see many instances of cervical endometriosis following dilatation and curettage, tracheloplasty, or trauma resulting from childbirth.

Conclusion and Summary

Sixteen cases of primary endometriosis of the cervix are reported. Our experience indicates that this lesion is not so rare as it is generally thought to be. Eight of sixteen patients had no symptoms; whereas the remaining eight had intermenstrual or postcoital spotting. The gross appearance of cervical endometriosis may vary as greatly as that of pelvic endometriosis. It may resemble carcinoma.

Twelve of the sixteen patients had had previous cervical operative procedures. We believe that this condition may result from transplantation of endometrial particles into punctures or lacerations of the cervix following surgical procedures, and possibly following childbirth trauma.

Cervical endometriosis will be diagnosed more frequently if cervices are carefully inspected, if biopsies are taken whenever indicated, if tissues are promptly placed in fixative, and if microscopic sections are carefully prepared.

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Discussion

DR. FRED O. PRIEST.—We are grateful to Drs. Ranney and Chung for pointing out to us that endometriosis of the cervix occurs more frequently than we have thought it did and much more frequently than we have diagnosed it. But, when compared with the occurrence of endometriosis in its more frequent sites, primary or even secondary involvement of the cervix must be considered rare. The common origin of the epithelium of the tubes, corpus, and endocervix makes metaplasia, under certain stimulation, a possible origin of the condition. Since experimental implantation has been so successfully carried out, then implantation of normal endometrium at the time of dilatation and curettage or of any other surgery whereby the cervix may be traumatized, or at delivery, must be considered other possibilities. Certainly the cervix, so ideally situated, is not a very receptive host or it would be the most common site of endometriosis. The absence of sterile conditions, the difference in the pH of the

vagina, plus the resistance of the intact squamous epithelium of the cervix probably account for the infrequency of the condition in such an ideal location. Many of us may have destroyed, by cauterization, small implants located just beneath the epithelium of the portio. Perhaps the report this evening may stimulate us to prove by biopsy the true diagnosis of some lesions that we might otherwise destroy or cure without a diagnosis.

Going through the cross index of pathology, 1941 to 1951, at the Presbyterian Hospital I found endometriosis of the cervix diagnosed in nine cases. Of these, microscopic sections were not available on three; on three others that I studied I could not diagnose primary endometriosis of the cervix because the sections were obviously taken from high in the cervix, were not covered by stratified squamous epithelium, and may have been a part of the picture of adenomyosis with secondary involvement of the cervix. So only three sections that I found really met the requirements of diagnosis. All of the sections mentioned were taken from the cervix after total hysterectomy—none from biopsy specimens.

DR. A. L. LASH.—The pathogenesis is very interesting. Here is a lesion that should occur more commonly since there is menstrual flow occurring every month over the cervix, with a very responsive stroma.

DR. RANNEY (Closing).—As Dr. Priest suggested, it is certainly possible that small lesions of cervical endometriosis have been cured by cautery or by biopsy.

Dr. Lash's implication, that the chief importance of this subject is to draw more careful attention to the cervix and to cervical biopsies, merits re-emphasis.

Dr. Greene's kind remark concerning the gross recognition of cervical endometriosis leads me to summarize my experience, based on the six lesions I have biopsied: Early cervical endometriosis looks like a "blood blister." It is bright red, velvety, slightly elevated, but covered with smooth squamous epithelium, often symmetrical, but not necessarily so. Just before, during, and just after menstruation the color of the "blood blister" may be the dark blue of "old" blood. Later, the lesions may ulcerate or become papillary, resembling cancer, or may show brownish staining from blood pigments. Rarely is there as much scarring as is usually found in pelvic endometriosis.

The age range of the sixteen patients, reported herein, was 25 to 60 years. The average age was 38.4 years.

Of the sixteen patients with primary cervical endometriosis, eight had major pelvic surgery. Six of these had pelvic endometriosis, confirmed microscopically. Of the eight in whom no major pelvic surgery was performed there was clinical evidence of pelvic endometriosis in three. Thus nine of the sixteen patients with cervical endometriosis also had microscopically proved or clinically manifested endometriosis elsewhere in the pelvis. The cervix is a poor site for development of endometriosis; reasons for this have been outlined by the authors and discussants. Otherwise, many more women having cervical or vaginal surgery, or dilatation and curettage would develop cervical endometriosis. The fact that all such patients in the reproductive age group do not develop cervical endometriosis, plus the high coincidence of other endometriosis among these patients who did develop cervical endometriosis, forces us to raise this question: Have the tissues of these women some particular physiologic characteristic which especially facilitates the growth of endometriosis?

Biopsies were sectioned, stained, and diagnosed in the Department of Obstetrics and Gynecology at Northwestern University Medical School.

COMBINED INTRAUTERINE AND EXTRAUTERINE PREGNANCY PROGRESSING TO TERM

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ONE of the rarest occurrences in obstetrics is combined intrauterine and extrauterine gestation at term. The purpose of this paper is to report such a case, review the literature, and discuss some of the aspects of this interesting syndrome.

Case Report

R. L., a white woman, aged 34 years, para iv-0-0-iv, was admitted to the hospital Aug. 22, 1951, with irregular pains which ceased shortly after admission. Her last menstrual period was Nov. 23, 1950. She was first seen on July 13, 1951, and was followed thereafter at regular intervals. On July 27, multiple pregnancy was suspected and confirmed by x-ray (Fig. 1). Two fetal hearts were heard throughout the remainder of her prenatal course. Her expected date of confinement was August 30. History of the present pregnancy was otherwise normal. Vaginal examination revealed the cervix to be 1 to 2 cm. dilated and very markedly displaced anteriorly beneath the symphysis. She was discharged with the diagnosis of pseudolabor, and was readmitted on August 28, this time in active labor. The abdomen was moderately distended with but one fetal heart audible. The height of the fundus was 31 cm. Rectal examination revealed 2 to 3 cm. dilatation of the cervix with the first twin presenting as right sacroposterior, the breech at the level of the spines. Membranes were ruptured on admission. Temperature, pulse, respiration, and laboratory findings were within normal limits. Labor progressed rapidly, and the patient was delivered of a normal 3,289 gram female infant two and one-half hours later by breech extraction under gas-oxygen-ether anesthesia. On vaginal examination, no sac was palpable. A placenta, lying free in the lower uterine segment, was removed. The uterus was explored and found to be empty and intact. A soft mass was palpated posterior and to the right of the uterus, with irregular masses deep in the epigastric region and under the right costal margin. The diagnosis of abdominal pregnancy was confirmed by x-ray (Fig. 2), and laparotomy was performed.

Operative Findings.—The fetus, partially macerated, lay in the oblique position with the head in the right upper quadrant (Fig. 3). The sac had been ruptured before operation and the placenta was adherent to the posterior part of the fundus uteri and the right broad ligament. The cord was tied close to the placenta, the infant removed, and the placenta left in situ. The operation was accompanied by minimal bleeding. The abdomen was closed without draining. The extrauterine fetus was a 1,758 gram female.

Course in Hospital.—On August 30, the patient developed bronchopneumonia. She was given antiobiotics, oxygen, fluids, and supportive therapy, and improved gradually in this respect, but became progressively more distended. On September 3, evisceration occurred. The wound was repaired with braided silk sutures, and continuous intestinal drainage was maintained. Symptoms gradually subsided thereafter. Lactation of moderate degree occurred on August 31, three days after operation. Friedman tests were positive as late as October 1, thirty-three days after operation. A Friedman test done six months after operation was negative. The patient has been asymptomatic since. Pelvic examination six months post partum revealed the placenta to be about 6 to 8 cm. in diameter.

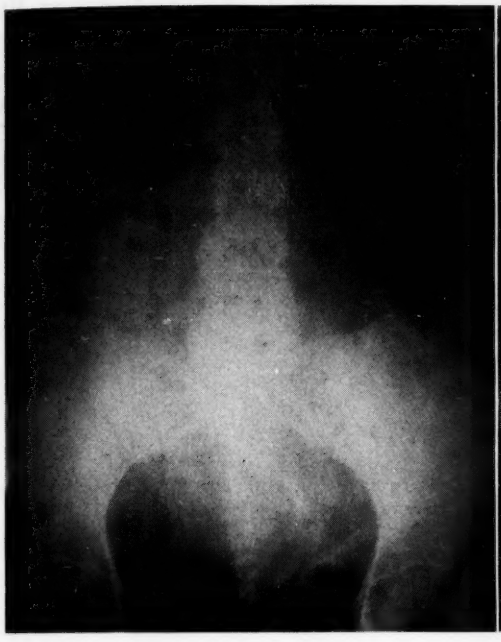

Fig. 1.

Fig. 2.

Fig. 1.—Flat plate of abdomen revealing multiple pregnancy.
Fig. 2.—Flat plate of abdomen immediately after delivery of the first twin.

Fig. 3.—Macerated fetus seen at operation, lying in right upper quadrant of abdomen. Sac was previously ruptured. The placenta was attached to the posterior portion of the fundus uteri and right broad ligament.

Review of the Literature

Heterotopic pregnancy in general includes all cases of combined intra- and extrauterine pregnancy, regardless of the time that either or both pregnancies terminated. This usually occurred in the first trimester.

TABLE I. RECENT CASES OF HETEROTO

NO.	AUTHOR	YEAR*	AGE (YEARS)	RACE	PREVIOUS PARITY	GESTATION (WEEKS)	WEIGHT OF INFANTS (GRAMS)		INTERVAL BETWEEN DELIVERIES	TYPE
							EXTRA	INTRA		EXTRA
1	Sunde[10]	(1919†) 1929	24	W	Nullipara	30	1,760	1,825	Immediate	parot-omy
2	Weintraub[11]	1931	38	N	Para ii Grav. ii	36	1,420	2,200	20 Hours	parot-omy
3	Bondurant[12]	1937	34	N	Para i Grav. iv	40	2,155	1,588	Immediate	parot-omy
4	Jabre[13]	1939	27	W	Para vi Grav. vi	38	? (Term)	? (Term)	15 Days	parot-omy
5	Leech[14]	1941	30	N	Para iii Grav. iii	40	2,722	2,495	21 Days	parot-omy
6	Rabago[15]	1944	32	?	Para viii Grav. viii	30	1,480	1,550	Immediate	parot-omy
7	Gilliland[16]	1949	35	N	Para v Grav. v	40	2,948	? (Term)	35 Days	parot-omy
8	Fejer and Henry[17]	1949	32	N	Para vi Grav. vi‡	40	? (Term)	? (Term)	24 Days	parot-omy

REGNANCY AT OR NEAR TERM (1925—)

TYPE OF DELIVERY		FETAL OUTCOME		MATERNAL OUTCOME	HISTORY OF PREGNANCY (IF RECORDED)	VAGINAL AND OPERATIVE FINDINGS	OPERATIVE PROCEDURE
EXTRA	INTRA	EXTRA	INTRA				
aparot-omy	Cesarean section	Neonatal death	Neonatal death	Lived	One day bleeding in first 8 weeks; RLQ pain; fainting	Sac not mentioned. Placenta on right adnexa and broad ligament	Attempt to remove placenta. Severe bleeding. No drainage
aparot-omy	Vaginal	(deformed)	Lived	Lived	Severe LLQ pain in third month—regular menses to seventh month	Sac intact. Placenta on descending colon and small bowel	Placenta left in; sac marsupialized. Drainage maintained. Placenta expelled through sac 24 days later
aparot-omy	Cesarean section	Lived	Neonatal death	Lived	Bled for one month in first trimester	Vaginal: Marked anterior displacement of cervix. Mass in cul-de-sac Sac intact. Placenta on left uterine wall	Placenta removed; severe. Bleeding requiring subtotal hysterectomy. Closure not recorded
aparot-omy	Vaginal	Lived	Stillborn	Lived	Not recorded. Sudden rupture of membranes and hemorrhage on day of delivery	Not recorded	Not recorded
aparot-omy	Vaginal	Neonatal death	Lived	Lived	Short menses to fourth month	Sac ruptured placenta on right broad ligament	Placenta removed easily. No undue bleeding. Closure not recorded
aparot-omy	Cesarean section	Neonatal death	Neonatal death	Lived	Severe lower abdominal pain in first trimester	Vaginal: No mention of position of cervix. Mass in cul-de-sac Sac ruptured. Placenta in cul-de-sac on posterior uterine wall	Placenta loosened; severe hemorrhage requiring subtotal hysterectomy. No drainage
aparot-omy	Vaginal	Lived	Lived	Lived	Not recorded	Sac intact. Placenta on left pelvic wall and in left iliac fossa	Placenta left in place. No drainage
aparot-omy	Vaginal	Neonatal death	Neonatal death	Lived	Not recorded	Sac intact. Placenta on anterior rectal wall and posterior uterine wall	Placenta removed; severe hemorrhage requiring subtotal hysterectomy. No drainage

TABLE—CONT

NO.	AUTHOR	YEAR*	AGE (YEARS)	RACE	PREVIOUS PARITY	GESTATION (WEEKS)	WEIGHT OF INFANTS (GRAMS) EXTRA	WEIGHT OF INFANTS (GRAMS) INTRA	INTERVAL BETWEEN DELIVERIES	TYPE EXTRA
9	Wiener and Carpenter[18]	1950	26	N	Para i Grav. i	40	2,098	2,722	9 Days	Laparotomy
10	Zarou	1951	34	W	Para iv Grav. v	40	1,758	3,289	One Hour	Laparotomy

*Date of report.
†Actual date of case.
‡Apparently normal deliveries at term. All died between 1-12 months.

The first recorded case was that of Duverney, found at autopsy, in 1708. Since that time, additions have continually been made in the literature by various authors. In 1902, Zinke[1] collected 88 cases, while in 1904 Simpson[2] found 113. Neugebauer[3] made an exhaustive study, and, in two series, claimed 244 cases existed in 1913. Novak[4] added 32 cases in 1926, making the total 276. Gemmel and Murray,[5] however, in 1933 were able to gather only 217 cases. They felt that numerous cases had been included which were not really eligible, such as twin pregnancy in a Fallopian tube or simultaneous pregnancies in both horns of a bicornuate uterus.

Using Novak's contribution as our source, we have traced the more recent additions. Mathieu[6] added 57 cases in 1936, and Ludwig[7] added 20 in 1938, making a total of 353 cases. DeVoe and Pratt[8] in 1947, using the figures of Mathieu[6] and Ludwig,[7] compiled 395 cases. We have reviewed the literature since that time and have been able to add 20 cases, including our own, making 415 cases existing in the literature to date. If Gemmel and Murray[5] be used as a source, the number would be approximately 357.

Novak[4] in 1926 found that of his 276 cases of heterotopic pregnancy at term, nine extrauterine babies were delivered alive at full term (Chrobak, Moore and Sale, Strathy, Wilson, Miller, Rumford, Bogdanovics, DuBose, and deAraujo). He states that there was a larger group in which both pregnancies continued to term with the delivery of a live intrauterine infant and operative removal of the dead extrauterine pregnancy, but elaborates no further on this. We have reviewed the literature since 1925 and have found 10 cases, including our own.

Incidence

DeVoe and Pratt[8] placed the incidence of heterotopic pregnancy in general at the Mayo Clinic at 0.015 per cent. Frank[9] estimates an incidence of one in every 105 ectopic pregnancies. Since the latter occurs about once in every 300 pregnancies, the frequency would be approximately one in every 30,000. To attempt to establish the incidence of heterotopic pregnancy at term would be almost futile, except to say that it would be unimaginably small.

TABLE I—CONT'D

TYPE OF DELIVERY		FETAL OUTCOME		MATERNAL	HISTORY OF PREGNANCY	VAGINAL AND OPERATIVE	OPERATIVE
EXTRA	INTRA	EXTRA	INTRA	OUTCOME	(IF RECORDED)	FINDINGS	PROCEDURE
Laparotomy	Vaginal	Stillborn	Lived	Lived	Severe cramps and bleeding in third and fourth months	Vaginal: Marked anterior displacement of cervix Sac not mentioned. Placenta on right posterior peritoneal wall	Placenta left in place. No drainage
Laparotomy	Vaginal	Stillborn	Lived	Lived	Negative	Vaginal: Marked anterior displacement of cervix Sac ruptured. Placenta on posterior right broad ligament and fundus uteri	Placenta left in place. No drainage

Comment

Ten cases, including our own, have been reported since 1925. The salient features of these are presented in Table I. Because the weight of the infant is not adequate in determining maturity in twin pregnancy, we have used rather the length of gestation as an index to how many of these patients actually went to term. Excluding the cases of Sunde[10] and Rabago,[15] both of 30 weeks' gestation, eight cases remain.

It is interesting to note that seven of the ten were in the 30- to 40-year age group, the average being 31.2 years. Furthermore, nine of the ten were multiparas. This conforms with the statistics of DeVoe and Pratt.[8] Six of the patients were Negroes, three were white, and the race of one was not recorded. MacGregor[19] has observed that abdominal pregnancy per se is more common in the Negro. This is probably due to the greater incidence of pelvic inflammatory disease in this group, coupled with their greater neglect in seeking medical aid in the first trimester when symptoms of tubal abortion or rupture are present.

The diagnosis in all cases was missed before delivery of the first twin. In the three in which cesarean section was done, it was stated that a mass palpable in the cul-de-sac would obstruct vaginal delivery. In five cases, the time interval between deliveries was between 9 to 35 days, illustrating the difficulty in diagnosis, even after the first delivery. Novak,[4] in 1926, stated, "So far as I know it has not been possible in any reported case to diagnose the presence of a living extrauterine and intrauterine child in late pregnancy or at term before the onset of labor. It is not until the birth of the uterine child that the presence or location of the extrauterine fetus is recognized. Expectant therapy would seem justifiable in cases in which two live embryos are recognized in later months, with the performance of abdominal section as soon as labor sets in." A possible modification of this would be elective section at about the thirty-eighth week to safeguard the extrauterine sac. A still more conservative viewpoint is that the diagnosis of abdominal pregnancy warrants immediate laparotomy, whatever the period of gestation. Error in diagnosis seems justified, in view of the rarity of the condition.

The signs of abdominal pregnancy per se were lacking in our case, and apparently in the cases reviewed. In the four cases subjected to vaginal ex-

amination, marked anterior displacement of the cervix was present in three. It would seem that this is a valuable sign in diagnosis, as has been pointed out by Cross, Lester, and McCain.[20]

The recorded weights of the fetuses ranged from 1,420 to 3,289 grams. The fetal mortality of the intrauterine fetus was 50 per cent, of the extrauterine fetus, 60 per cent. In seven cases in which the extrauterine sac was mentioned, it was intact at operation in four. In these four cases, three of the infants survived. Of the three remaining cases in which the sac was ruptured, the fetal mortality was 100 per cent. We can only speculate that the extrauterine sac in our case ruptured at the time of the first admission when the diagnosis of pseudolabor was made. There were no maternal deaths. According to DeVoe and Pratt[8] the maternal mortality in heterotopic pregnancy in general was nineteen per cent before 1940, and 1.4 per cent thereafter. This indicates that the maternal danger in this condition is greater in the first trimester than at term, due to the severe hemorrhage accompanying rupture of the extrauterine gestation. Although seven patients delivered vaginally, there was no clinical signs or evidence at laparotomy of extrauterine placental detachment, which apparently could easily occur. In these cases, labor had no appreciable effect on the implantation of the extrauterine placenta.

In five of the seven cases in which a prenatal history was recorded, there was bleeding in early pregnancy and in the sixth there was an episode of severe pain.

In five cases, the operator attempted to remove the placenta. In four of these, severe hemorrhage occurred, three of which required subtotal hysterectomy, and the fourth packing. In four cases, the placenta was left in, and in one, no mention of it was made. Cross, Lester, and McCain[20] emphasize the hemorrhage and morbidity that are produced by disturbance of the intra-abdominal placenta.

Although in our case lactation was not inhibited, chorionic hormone was found in the urine for 33 days. An interesting collary of this was MacGregor's[21] case, in which the Friedman test and blood prolan and estrin determinations became negative in a short time, and yet lactation did not occur.

Summary and Conclusions

1. A case of combined intrauterine and extrauterine pregnancy at term is presented.

2. A review of the literature of heterotopic pregnancy in general is given. We have found 20 cases, including our own, since 1947, making the total 415 cases.

3. A review of the literature of heterotopic pregnancy at term is given from 1925 through 1951. Eight cases, including our own, have been found, plus two at 30 weeks' gestation, the salient features of which are given in Table I.

4. Heterotopic pregnancy at term is discussed regarding age, race, parity, diagnosis, fetal and maternal mortality rates, and operative treatment.

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400 ONE HUNDREDTH STREET

UTERINE CANCER DIAGNOSIS*

Relative Accuracy of Vaginal Smear and Sponge Biopsy Techniques

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IT HAS been shown repeatedly that the diagnosis of uterine cancer can be made with a high degree of accuracy either with the Papanicolaou smear or with the Gelfoam sponge biopsy techniques.[1, 2, 3] However, most of these studies have been concerned either with surveys of groups of asymptomatic individuals[4] or with those known to be composed largely of cancer-positive individuals.[5] It is almost inevitable that these groups should have a high percentage of positive correlation because of: (1) the high percentage of negative cases in the detection group series and (2) the incalculable effect of guided study in the known positive cases.

The purpose of this survey was the evaluation of the relative efficiency of the vaginal smear and the Gelfoam sponge biopsy in the detection of gynecological cancer under routine working conditions in a tumor clinic. The patients were those seen consecutively in the gynecological section of the Meadowbrook Hospital Tumor Clinic, or in consultation on the wards of this hospital during the period of study. Objectivity was maintained: (1) by having specimens taken by the regular but changing group of examiners in the clinic after demonstration of the techniques by one of the authors (H. L. W.) in the interest of uniformity; (2) by treating all specimens as part of the routine general pathological examination without special attention being focused upon them; (3) by eliminating from the study all cases in which a satisfactory final clinical diagnosis could not be made, either because of inadequate follow-up or for any other reason. In this connection, we feel that the lack of follow-up or establishment of a final diagnosis by confirmed operative and pathological examination invalidates or weakens certain of the statistical studies obtained by cancer detection groups.

Material and Methods

The vaginal smears were taken by aspiration with a glass pipette from: (a) the posterior fornix, and (b) the external os, and smeared on one glass slide for each area aspirated. These slides were immediately immersed in a solution consisting of equal parts of 95 per cent alcohol and ether. In patients with profuse vaginal secretion, the excess was sponged away gently with gauze before aspiration.

*This study was conducted on patients attending the Meadowbrook Hospital Tumor Clinic, Hempstead, N. Y., under the direction and encouragement of Dr. Norman Treves, Clinical Director.

The Gelfoam sponge biopsy was obtained by rotating the sponge on a long uterine forceps within the cervical os so that all surfaces of the sponge were exposed to contact with cervical secretions. The Gelfoam sponge, Upjohn, was used, cut into 2 cm. squares.

All cases in this study were referred to the clinic or hospital by local physicians because of symptoms or findings which they felt required further investigation. This would make inevitable the inclusion of a fairly high percentage of positive cases. There were 320 cases studied, of which 50 were considered incompletely studied and discarded. There were no positive tests in any of these cases, but some were reported as suspicious. Of the remaining 270 patients, a diagnosis of gynecological cancer was made by biopsy and confirmed by either operation or autopsy in 35 cases.

These are divided as follows:

Cancer of the cervix uteri	26
Adenocarcinoma of fundus uterus	3
Sarcoma of uterus	2
Melanosarcoma of vulva	1
Vaginal cancer (post operation and radiation on cancer of cervix)	1
Epidermoid cancer of vulva	2

The results were reported as positive, suspicious, or negative. Only negatives were considered complete misses statistically, as suspicious reports resulted in continued study by all possible means until a final diagnosis was established.

TABLE I. RESULTS OF THE PAPANICOLAOU SMEAR AND GELFOAM BIOPSY

	POSITIVES	SUSPICIOUS	MISSED
All Neoplastic Cases, 35, Uterus, Vagina, and Vulva.—			
Vaginal smear	18	5	12
Gelfoam	11	2	22
Cancer of Cervix Only, 26.—			
Vaginal smear	15	2	9
Gelfoam	10	2	14
Miscellaneous Neoplasms, 9, Fundus Uteri, Vagina, and Vulva.—			
Vaginal smear	3	3	3
Gelfoam	1	0	8

The miscellaneous group consisted of all neoplasms of the uterus, vagina, or vulva, except those classified as cancer of the cervix uteri. Among the 9 miscellaneous cases, the vaginal smear was negative in 3 cases and the Gelfoam sponge biopsy was negative in 8. The only positive Gelfoam test in this group was in a uterine sarcoma (Case No. 8655). In the only other uterine sarcoma in the series (Case No. 9231), the first vaginal smear report was suspicious and the Gelfoam was negative. However, repeated tests were negative or equivocal also, and the biopsies were repeatedly negative or inconclusive although the tumor was invading the vaginal vault extensively at this time. Following removal of the tumor, these discrepancies were readily explainable because the tumor surface showed extensive necrotic changes. The 3 cases of adenocarcinoma of the fundus uteri were missed completely by the Gelfoam method, while the vaginal smears were reported as negative once, and suspicious in the other two.[2]

There were 26 cases of carcinoma of the cervix uteri. Nine of these were missed by the vaginal smear, and 14 were missed by the Gelfoam technique. Among the 9 negative vaginal smears in positive cases, were: (1) necrotic material, 1 case; (2) poor specimen due to vesicovaginal fistula, 1 case; (3) diagnosed as adenocarcinoma of the fundus uteri until after hysterectomy, 1 case;

(4) two cases in which the biopsy also was negative initially. In one, the diagnosis was established by dilatation and curettage. In the other (R. T.) repeated biopsies, hysterectomy, and careful examination of abdominal wall metastases always gave a benign impression pathologically, although the patient succumbed because of cancer of the cervix three months later.

There were two false positive vaginal smear reports. The biopsies in these cases were reported as: (1) Intraepithelial cancer, and (2) endocervicitis with precancerous epithelial changes. On repeated biopsies, the diagnosis was chronic endocervicitis in both cases, on two successive occasions. There were no false positive Gelfoam tests. Three of the false negative Gelfoam tests were reported as unsatisfactory specimens.

Thus, of 270 cases in the series, there were 12 cases in which the vaginal smear report was negative, but the final diagnosis was malignant disease of the uterus or vagina. There were 22 such cases among the Gelfoam group. There were 2 false positive vaginal smears and no false positive sponge biopsy reports.

The absolute reliability therefore can be considered as 95 per cent for the vaginal smear, and 91.9 per cent for the Gelfoam sponge biopsy for the whole group studied. However, if proved cancer of the cervix cases only are considered, the positive correlation is only 66.4 per cent for the vaginal smear method, and 46.2 per cent for the Gelfoam sponge.

The difference, of course, reflects the high percentage of negative cases that are included. This factor becomes of much greater significance when surveys are conducted on completely unsuspected groups, as the expected incidence of less than 2 per cent would result in a 98 per cent accuracy even if all cervix cancer cases were missed. Even if only positive cases detected by any means in such large group studies are compared with cytological test results, the true accuracy can never be established, as the clinically negative cases missed by smear techniques may not be detected for years, and may never find their way into the recorded statistics of the group under study.

In those groups reporting highly accurate correlations in a series of patients thoroughly studied, and with the final diagnosis established, the results were aided by several factors: (1) Many slides were taken and thoroughly studied by specially trained investigators.[6] (2) The results were classified pathologically in categories that eliminated many of the most difficult cases to diagnose by cytological means.[6] (3) Repeated tests were taken where lack of correlation was suspected.[5] This distinction is exemplified by the report of Scheffey and associates[7] who, in a somewhat comparable group of cases (500 studied, 63 uterine cancer in the group), found a positive correlation of 70.2 per cent in cancer of the cervix, and 66.7 per cent in cancer of the fundus when only positive cases were considered. Their technique consisted of the study of a single smear prepared after aspiration of the posterior vaginal fornix.

It should not have been difficult to increase the accuracy of both of these tests in our series by special treatment of the cases either by repetition of tests and including positives in the final recordings or by recutting of the Gelfoam sections. Additional specimens taken because of the stimulated interest from other positive findings, either clinical or pathological, did result in more positive correlations, but these are not included in our statistics. Our purpose was not to show how accurate can be the results obtained under the best circumstances as this has been well shown by the original investigators. Our purpose, rather, was to show: (1) The relative accuracy of the two tests, and (2) the absolute reliability of the tests under ordinary working conditions such as would apply generally in the surveys on unsuspected cases when no follow-up would be done on negatively reported cases.

Results

In our series, the vaginal smear method proved 50 per cent more reliable than the sponge biopsy. In only one case did the sponge technique result in a correctly positive test, where the vaginal smear report was negative, but the reverse was true in four cases.

Conclusions

1. A series of 270 consecutive cases have been examined in the gynecological section of a tumor clinic by the vaginal smear and the sponge biopsy techniques, and checked against biopsy, operative, and follow-up results.

2. The over-all group positive correlation was 95 per cent for the vaginal smear, and 91.9 per cent for the sponge biopsy.

3. In cases of proved cancer of the cervix uteri, the positive correlation was 66.4 per cent for the vaginal smear and 46.2 per cent for the Gelfoam sponge biopsy.

4. No case of carcinoma of the fundus uteri was correctly diagnosed by the Gelfoam technique, while one of three cases was missed by the vaginal smear method.

5. The vaginal smear was 50 per cent more accurate than the Gelfoam sponge biopsy in the diagnosis of cancer of the uterine cervix.

6. A negative report by either method does not lessen the necessity for further study in clinically suspicious individuals.

7. A positive report by either method greatly increases the probability of an ultimate diagnosis of cancer.

8. Highly accurate results may be obtained only when multiple or repeated studies are made by well-trained investigators.

9. The vaginal smear and Gelfoam sponge biopsy are valuable additions to our techniques in the study of gynecological cancer, but cannot replace a complete study. Their chief value lies in the focusing of all our diagnostic faculties on the otherwise unsuspected case.

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3096 NORTHERN BOULEVARD.

RADIATION THERAPY IN MENSTRUAL DISORDERS AND STERILITY

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THE value of roentgen-ray therapy as an adjunct in the treatment of menstrual irregularities and for sterility is still controversial. Van de Veldon[1] was one of its earliest advocates. Applying the concept of the Arndt-Schultz law of pharmacology to radiation therapy, he reasoned that "small doses of x-ray stimulate, moderate doses inhibit, and large doses destroy vital processes." On this theoretical basis, he employed small doses to the ovaries of women suffering from menstrual disturbances and obtained return of normal function. Collins[2] stated that, in his experience, radiation is the method of choice in anovulatory secondary amenorrhea, increases the chance of pregnancy sixfold after the restoration of normal periods in all types of patients, and is especially indicated under the age of thirty. Mazer and Cheek[3] believed that low-dosage irradiation of the pituitary and ovary offered the most effective, quickest, and least expensive method of restoring normal rhythm and fertility.

The principal objection to radiation therapy in sterility and menstrual disturbances has been the fear of causing damage to the ovaries or to the offspring of the treated or future generations.

Collins, in an analysis of data obtained through a questionnaire submitted to 410 gynecologists, found that 70 per cent (290) would not employ this method, mainly because of this fear. However, 30 per cent (120) used radiation therapy. They treated 4,200 patients for sterility and found no harmful results either to the patient or to subsequent pregnancies. Haman[4] claimed that medical literature lacks one authentic proved instance of damage in a case of sterility treated with low-dosage irradiation.

Menstrual disturbances and sterility are two problems frequently encountered in gynecological practice and are often interwoven. Rubin[5] from personal experience with over 10,000 patients, including both private practice and ward cases, estimated that absent, delayed, or irregular menstruation occurred in 8 per cent and that the women with normal menstruation had a fivefold better chance of becoming pregnant. He also found that among married women, 15 to 20 per cent were sterile and incapable of conception. Finkler[7] claimed involuntary sterility occurred in 17 per cent of all marriages. It was due to the female in 50 per cent, to the male in 40 per cent, and to both in 10 per cent.

Material

In an effort to obtain information about the value of low-dosage irradiation therapy for menstrual disturbances and sterility, 39 patients were studied.

Eight patients, ranging in age from 15 to 27 years, had cases of menstrual irregularity only; 31 were sterility problems, with or without menstrual irregularity, with an age range of 20 to 34 years. The average period of infertility was five years and the extremes were 2 to 10 years.

The investigation of the infertile group conformed to the minimal standards of the American Society for the Study of Sterility, including analysis of the husbands' sperm. Endometrial biopsies were obtained within five days of the expected menstrual period by means of the Novak curette. If the expected period was delayed beyond five days after biopsy, the test was repeated at a later cycle. The microscopic evaluation of the endometrial tissue was done by a general pathologist who had no further knowledge of the cases. Biopsies were not taken among the 8 treated only for menstrual disturbance.

Each patient received treatment to both the pituitary gland and the ovarian regions. Each area was given a total of 150 r in air of deep quality radiation (200 kv., ½ copper and 1 aluminum, 50 cm. skin target distance, 20 Ma.) over a period of two weeks. A 5 cm. portal was used over each lateral pituitary region and a 10 by 10 or 10 by 15 cm. field was used for the anterior and posterior aspects of each ovarian region. The total tissue dose for the pituitary gland was estimated to be approximately 90 r at 5 cm. depth, while the tissue dose for the ovaries was estimated to be approximately 80 r at 6 cm. depth. For protracted radiation in divided doses, the total amount of radiation is quite small and its tissue effect is minimal. None of the patients experienced any symptoms of clinical radiation sickness.

The results obtained among the patients with the menstrual disturbances were satisfactory in 7 of the 8 cases, or 87.5 per cent. The menstrual periods became regular and normal after completion of the irradiation. Periods remained irregular in one patient. Two of these patients subsequently conceived, and delivered normal infants.

Results

Results of the 31 irradiated patients of the infertility group were as follows:

CASES	PRETHERAPY BIOPSIES	POSTTHERAPY BIOPSIES	PREGNANCIES	PERCENTAGE
9	9 Proliferative	9 Secretory	6	66.6%
6	6 Secretory	5 Secretory	3	50%
	(One became pregnant during treatment)			
6	6 Proliferative	6 Proliferative	0	
2	2 Proliferative	None	2	
	(Became pregnant cycle following treatment)			
3	None	None	3	
	(Too irregular to predict periods, 2 became pregnant the cycle following treatment, 1 during treatment)			
5	5 Proliferative	None	Failed to return	
31			14	45.1%

Since 5 patients conceived before posttherapy biopsy could be obtained, it is reasonable to assume that they had developed secretory endometrium after radiation. Therefore the percentage of conversion to a completed endometrial cycle would be higher than indicated above.

All but one of these women became pregnant within nine months following therapy.

Four patients have been delivered of a second pregnancy, making a total of 17 infants born of these mothers. One pregnancy is undelivered at this writing. Two pregnancies terminated in spontaneous abortion (10 per cent).

Special note is taken of the two patients who conceived during the cycle in which they were receiving low-dosage irradiation. No mental or physical abnormality could be demonstrated in the infants subsequently delivered of these two pregnancies. The other children of term pregnancies likewise showed no abnormal manifestations, nor was harmful effect noted in any of the 39 patients who were irradiated. However, it could be demonstrated in 6 cases (19.4 per cent) of the infertility group that irradiation failed to make any change in the endometrium and these women did not conceive.

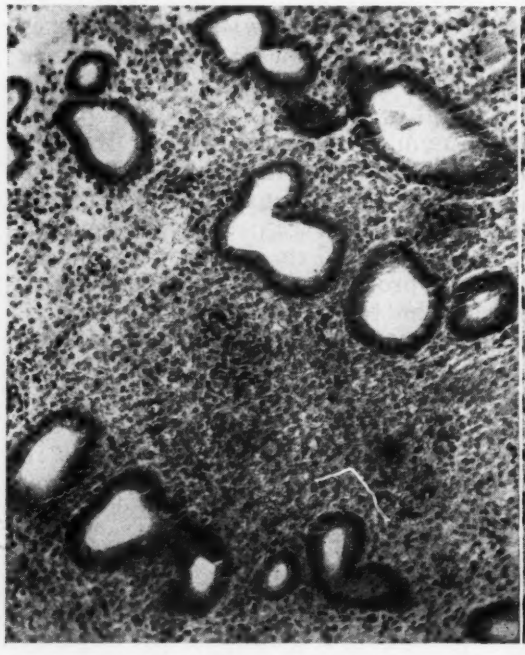

Fig. 1.

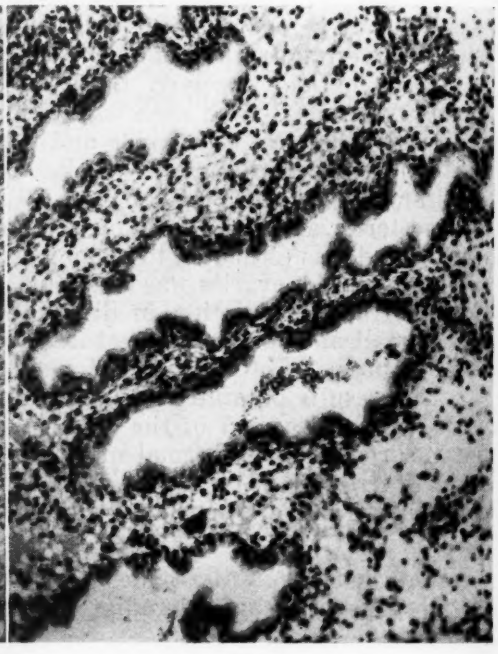

Fig. 2.

Illustrative Case Reports

CASE 1.—W. B., aged 21 years, married five years.

General history, physical and pelvic examinations were negative except for history of rheumatic fever in childhood. Menstrual history indicates periods of irregularity of the menstrual cycle alternating with regular periods.

The husband's sperm analysis was within normal limits. Huhner test showed fair motility of sperm in cervical mucus. Kurzrok-Miller mucus penetration test demonstrated good penetration. The Rubin test revealed tubal patency.

Feb. 28, 1948: Endometrial biopsy had appearance of proliferative endometrium (Fig. 1).

June 2, 1948. Low-dosage irradiation of pituitary and ovaries completed.

July 24, 1948: Repeat endometrial biopsy showed secretory endometrium (Fig. 2).

July 1, 1948: Last menstrual period before pregnancy.

April 4, 1949: Delivered normal male infant, weighing 7 pounds, 2 ounces.

May 9, 1950: Last menstrual period before pregnancy.

Feb. 18, 1951: Delivered normal male infant, weighing 7 pounds, 7 ounces.

CASE 2.—R. F., aged 28 years, married seven years.

General history and physical examination were negative except that patient had an exploratory laparotomy and appendectomy five years previously. Menstrual history re-

vealed irregular cycles and amenorrhea for the preceding eight months. Pelvic examination was negative except for a small uterus.

The husband's sperm analysis showed a good specimen. Huhner test revealed no living sperm in three hours. Kurzrok-Miller mucus penetration test demonstrated good penetration. The Rubin test indicated tubal patency.

Nov. 3, 1948: Endometrial biopsy revealed proliferative endometrium (Fig. 3).

April 15, 1949: X-ray stimulation of pituitary and ovaries completed. Menstrual periods began with fair degree of regularity.

Aug. 13, 1949: Endometrial biopsy showed secretory endometrium (Fig. 4).

Dec. 26, 1949: Last menstrual period before pregnancy.

Sept. 22, 1950: Delivered normal female infant, weighing 6 pounds, 9 ounces.

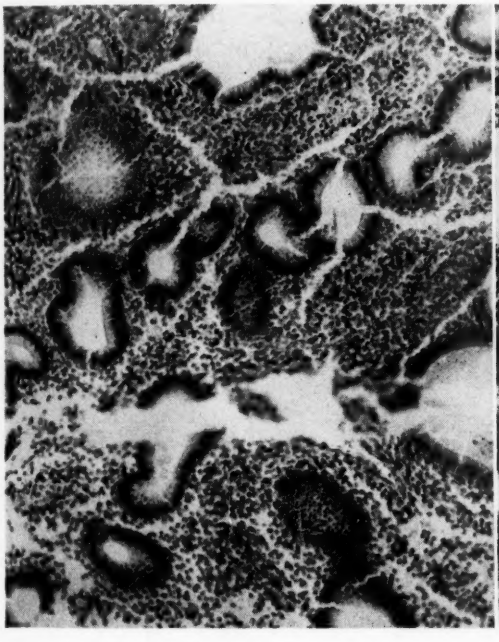

Fig. 3.

Fig. 4.

Summary and Conclusion

1. Low-dosage irradiation for menstrual disorders in young women is clinically safe and gives a high percentage of good results.

2. Low-dosage irradiation appears to be a safe and helpful procedure in the management of female sterility.

The prognosis for the success of radiation therapy appears to be reflected to a significant degree by the phase of the endometrium as shown in biopsies taken the last few days of the menstrual cycle, and indicates that endometrial conversion from a persistent proliferative to a completed endometrial cycle can be accomplished by this method.

3. Two cases are noted in which low-dosage x-ray irradiation was administered during the cycle in which they conceived without demonstrable abnormality in the infants delivered of these pregnancies.

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THERAPEUTIC EFFECTS OF METHYL ANDROSTENEDIOL*

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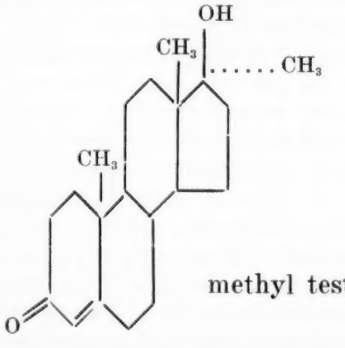
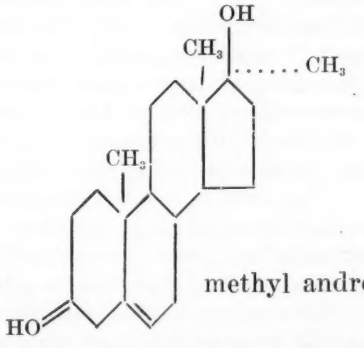
IN WOMEN there are various clinical disorders based upon endocrine imbalances in which it is desirable to employ androgen (male hormone) therapy to provide an anabolic or protein-building action, to counteract the effects of estrogens, or to suppress excessive pituitary gonadotrophic function and the autonomic effects that occur in the menopause. Although testosterone[7] has been widely employed for these therapeutic actions, yet its tendency to produce virilization stigmas in women is so pronounced that the usefulness of testosterone is limited and must be cautiously watched. Methyl androstenediol† has a good many of the actions of testosterone without having such pronounced masculinization tendencies, and for this reason its use is being explored in various conditions in which testosterone has been useful in women.

Methyl androstenediol has a chemical structure quite similar to that of methyl testosterone, as shown in the following structural formulas:



methyl testosterone



methyl androstenediol

Its androgenic action in test animals as listed in Selye's *Encyclopedia of Endocrinology*[8] is very much less than that of methyl testosterone. Homburger and associates[5, 5a] have reported that this steroid, like testosterone, has produced palliation of breast cancer, and virilization has only occasionally been elicited even with very large doses of methyl androstenediol (as much as 100 mg. daily), employed for months. Several investigators[3, 5, 6, 9-12] have shown in metabolic balance studies that this steroid produces a protein anabolic action. Goodman and Kupperman[2] have reported that methyl androstenediol given before ovulation was effective in relieving dysmenorrhea, without at the same time suppressing ovulation. Hall[4] has reported favorable results with methyl androstenediol in mastopathy, premenstrual tension, "hyper-

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†The methyl androstenediol employed was supplied by Organon, Inc., under the trade name of Stenediol.

estrinism," and "physical exhaustion" of women, and concluded that methyl androstenediol therapy accomplished what testosterone does, but with less tendency to virilization.

Material

The present report will describe my experience with methyl androstenediol therapy to alleviate menopausal symptoms, mastopathy, and dysmenorrhea, and to suppress lactation. This study was undertaken with a view of exploring the possible usefulness of this relatively new steroid, and the results in the first forty-eight patients are presented as a preliminary report. In many of the women in whom the methyl androstenediol was employed there was reason to avoid estrogen. This situation is becoming increasingly a problem for the gynecologist, for it is clearly undesirable to employ estrogen therapy in women who have malignant tumors of the breast or reproductive tract, or even in those in whose families these malignancies are common. Also, there is increasing tendency to avoid estrogen therapy in the group of women in whom the Papanicolaou smear and other clinical evidence indicates "hyperestrinism." In this group are included women with endometriosis, fibroids of the uterus, and mastopathy. In most of these patients, androgen therapy is usually preferred.

Twenty-five women having typical menopausal symptoms were studied. This group was selected to receive this particular steroid because in most of the individuals estrogen therapy for one reason or another was undesirable. For example, seventeen had fibroids, one had mastectomy for cancer, and several had clinical and cytological signs of "hyperestrinism." All were observed sufficiently carefully to evaluate the results. In the majority of the patients, flushes were the outstanding symptom, but in others mental depression or tender joints of the fingers were prominent symptoms.

The methyl androstenediol was usually administered intramuscularly as a microcrystalline aqueous suspension in doses of 25 mg., and this was repeated at intervals of two or three days until relief was obtained. Injections were then stopped and resumed if symptoms reappeared. Some patients obtained relief of symptoms after a single injection and others after only two injections. The results of the treatment were as follows: Twelve patients reported complete relief; ten, marked relief; three, no improvement. Several of these patients had been treated with estrogen and others with testosterone before this new steroid became available, and in three instances (Cases 12, 18, and 21) the methyl androstenediol was apparently inferior to estrogens in its effect on the menopausal symptoms, for the patients reported greater relief from estrogen therapy. On the other hand, there were two instances (Cases 23 and 24) in which this steroid gave results superior to the effect of estrogens, and both of these women's symptoms followed ovariectomy. Estrogens had relieved one woman's flushes, but had not influenced her frigidity. However, with methyl androstenediol not only were the flushes relieved, but also the frigidity. This patient stated that she ". . . felt the urge to have intercourse for the first time in my life."

The anti-estrogen effect of methyl androstenediol therapy was studied in a few of the menopausal patients by comparison of vaginal smears stained by the Papanicolaou method. Examples are as follows: A 44-year-old woman (Case 9) with fibroids, menorrhagia, secondary dysmenorrhea, and possible endometriosis showed a suppression of estrogen effect in the vaginal smear after 100 mg. of methyl androstenediol in four injections. Similarly, a 39-year-old woman (Case 10) who suffered from secondary dysmenorrhea and menorrhagia and who had palpable fibroids, also showed hyperestrinism. She received a total dosage of 350 mg. of methyl androstenediol during a period

of four months, after which time the vaginal smear showed "hypo-estrinism" and androgen effects. The endometrium was in the proliferative stage at this time.

The superiority of methyl androstenediol over testosterone was apparent in three of the patients (Cases 6, 8, and 15). These women had previously shown signs of virilism while receiving testosterone therapy, but these virilizing effects failed to reappear during methyl androstenediol therapy in two of these patients. In one, this undesirable effect did seem to reappear somewhat, but was noticeably less than before with testosterone treatment.

Nine women having dysmenorrhea were treated with methyl androstenediol. In five of these the treatment was begun in the preovulatory portion of the cycle, following the method of Filler[1] and of Goodman and Kupperman.[2] Beginning just one week prior to the estimated time of ovulation, the patients received 25 mg. of methyl androstenediol buccally from one to three times daily for seven days. In four other cases the treatment was begun just prior to the onset of the menses, and injections of 25 mg. of the steroid were given on days when pain was present.

The results in both groups of cases (the preovulatory and the premenstrual) were strikingly successful. In the preovulatory group, the larger dose, 25 mg. three times daily, was successful in all five. One patient received no relief in the second month of treatment with a total dosage of 175 mg. but did receive relief in the first and third months with a total dosage of 350 mg. in each month. Another patient received no relief in the first month with the total dosage of 175 mg., but did obtain relief in the second month with a total dosage of 350 mg. During two subsequent months she had no dysmenorrhea, and had no further treatment. One patient was completely relieved with a total dose of 350 mg. administered buccally.

In the premenstrual group, from one to three injections of 25 mg. each was sufficient to prevent pain during the approaching menses.

Seven women having cyclic mastopathy were treated with methyl androstenediol. The disturbance was characterized by the presence of nodular masses which became tender at the time of or shortly before the menstrual period. Two of the women also had premenstrual tension and two had evidence of "hyperestrinism." The treatment in five was 25 mg. of methyl androstenediol in aqueous suspension injected intramuscularly daily beginning three or four days prior to the onset of menses. In two, the steroid was given buccally. The results in six of the patients were excellent, with very satisfactory relief of the tenderness and some apparent reduction in the nodular quality of the breasts. One woman who received a total buccal dosage of 350 mg. thought she detected some signs of darkening of the hair of the upper lip, and in this same patient the libido sexualis improved considerably. One patient had no relief at all of the mastopathy symptoms following a dose of 25 mg., nor again after 100 mg. in a single injection and this latter dosage was painful.

Eight women were treated with methyl androstenediol in an effort to suppress lactation. The treatment of five was begun on the first day post partum, but three were treated after they had nursed their babies for one-half, one, and two months. (The treatment was 25 mg. three times a day for three to four days, buccally.) Seven of the eight women experienced excellent results with satisfactory suppression of lactation, but one developed congested breasts on the sixth day and had to be treated by conventional methods.

Comment

The treatment with methyl androstenediol in these four conditions was in general considered satisfactory for the purposes intended. Indeed, in view

of the lack of virilizing symptoms during this therapy, this steroid proved to be more useful than testosterone. These studies which are not extensive enough to represent a full appraisal of the effectiveness of this drug, nevertheless indicate that this steroid is worthy of wider investigation for therapy in these conditions.

One observation deserves special mention; this concerns withdrawal bleeding which is one of the undesirable complications of estrogen therapy. This disturbance occurred in three of the women treated with methyl androstenediol; two were menopausal women with fibroids of the uterus, one had been treated for suppression of lactation. It is conceivable that the bleeding in all three of these patients was due to some other cause, but the interval of five to seven days was characteristic of withdrawal bleeding, and it is suggested that this possibility be borne in mind in future case reports. The smallest dosage of methyl androstenediol preceding this symptom was a total of 100 mg. administered in two injections on two consecutive days.

The only trace of virilizing action due to the methyl androstenediol therapy in the forty-eight patients was a slight darkening of the hair of the upper lip of one of the mastopathy patients, but this effect was considerably less with a monthly dosage of 150 mg. of methyl androstenediol than it was with a monthly dosage of 75 mg. of methyl testosterone. Two other women who had developed definite virilizing symptoms with testosterone showed none of these symptoms with methyl androstenediol. In two of the women there was rather definite evidence of relief of the symptoms of frigidity following methyl androstenediol treatment.

Summary

Forty-eight women having endocrine disturbances in which androgen therapy is useful were treated with methyl androstenediol. The therapy was either intramuscular injections of from 25 to 50 mg. of an aqueous microcrystalline suspension, or oral or buccal therapy with tablets of the steroid in daily doses of 25 to 75 mg.

Twenty-five women having well-established menopausal symptoms were treated, and twelve had complete relief of symptoms; ten reported marked improvement; three had no relief and these women preferred the effects of estrogens.

Nine women having dysmenorrhea were treated; in five, the treatment was started at the preovulatory period, and in four, at the onset of menstrual molimina. This treatment was successful in all of these patients, but it was strikingly successful and convenient in the patients treated in the preovulatory period, for these patients were successfully treated with oral tablets; those in the other group were given injections. In the preovulatory treatment, a total dosage of 350 mg. during a period of seven days appeared to be required, for a dose of 175 mg. gave no relief in two instances.

Eight women were treated to suppress lactation, and the results were excellent in seven; in an eighth case congestion developed and the steroid treatment was adjudged a failure. This patient had been nursing her baby for a month prior to starting the treatment.

Seven women having mastopathy were treated, and two of these patients also had premenstrual tension. The results were excellent in six. One woman experienced no relief of symptoms after a single dose of 25 mg., nor after 100 mg. in a single dose, and this last injection was painful.

These experiences with methyl androstenediol lead to the conclusion that this steroid warrants wider investigation, and offers considerable promise as a substitute for testosterone therapy in women.

Addendum.—Since this paper was written eight additional women were treated with methyl androstenediol using the same method for suppression of lactation and in all eight cases lactation was satisfactorily suppressed.

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AMNIOTIC FLUID EMBOLISM

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AMNIOTIC fluid embolism has been adequately reviewed in the literature since it was first described by Steiner and Lushbaugh in 1941. Notwithstanding the fact that this disorder is now a well-recognized entity, it is a sufficiently rare syndrome that individual case reports are worthy of publication.

Contact with a fatal case of amniotic fluid embolism by one of us (C. W.) stimulated our interest to ascertain the exact cause of death. Previous writers have conjectured that these patients succumb to a fatal "anaphylactoid reaction."[6, 10, 27, 28] The series of experiments described in this publication were designed to test the validity of this opinion.

Case Report

No. 9454. Mrs. E. M. was a 39-year-old gravida ii, para i, who entered St. Joseph's Hospital on Sept. 16, 1948, for induction of labor. Her expected date of confinement was Sept. 9, 1948, and, on questioning, it was found that her pregnancy had been uneventful.

On admission the blood pressure was 130/90, pulse 80, temperature 99.2° F., and respiratory rate 16. The position of the fetus was left occipitoposterior and the fetal heart rate was 124 per minute. Rectal examination revealed the presenting part at a minus 1 station and a ripe cervix with 2 cm. dilatation. Urine examination was negative.

At 10:35 A.M. 2 ounces of castor oil were given and this was followed by 10 c.c. of 10 per cent calcium gluconate intravenously. At 1:20 P.M. the membranes were ruptured artificially. Shortly thereafter contractions became regular and at 2:15 P.M. the pains were severe every two to three minutes, lasting 40 seconds. Sedation consisting of Seconal, 3 grains, Demerol, 100 mg., and scopolamine, 1/150 grain, was given. At 3:50 P.M. the cervix was 6 cm. dilated and the patient was removed to the delivery room. Suddenly at 4:00 P.M. she became dyspneic and cyanotic. In spite of oxygen she was soon gasping. Within five minutes respiration ceased but a rapid, thready pulse could still be palpated. Treatment consisted of oxygen, artificial respiration through an endotracheal tube, and stimulants. In spite of vigorous therapy the patient died undelivered at 4:10 P.M.

Postmortem: The examination was performed by Dr. W. A. D. Anderson, attending pathologist. Pertinent findings were limited to the lungs. The right and left lungs weighed 290 and 265 grams, respectively. Microscopically the lungs showed focal areas of atelectasis and emphysema. Polymorphonuclear leukocytes and a few lymphocytes were seen within the alveolar walls. The small arterioles contained epithelial squamae, meconium, and acidophilic granular material. Leukocytic infiltration of the vessel walls was demonstrable. No laceration was found in the uterus or cervix.

Materials and Methods

In the authors' series of experiments the rabbit was chosen as the experimental animal because the syndrome can be duplicated in rabbits. All animals were adult rabbits weighing from 5 to 8½ pounds. Two animals were used for each experiment. The animals which succumbed to the experiments were immediately autopsied and the tissues fixed in formalin and stained with hematoxylin and eosin stain. Rabbits which survived the experiments were sacrificed by the intravenous injection of 50 mg. of Nembutal per 5 pounds of body weight into the marginal vein of the ear. The animals were then autopsied

and the tissues fixed and stained in the same fashion. In instances in which anesthesia of the animal was required (Experiments 4, 5, 6, and 7) Nembutal, 50 mg. per cubic centimeter, was slowly injected into the marginal ear vein until the rabbit barely reacted to painful stimuli.

All organs of the thorax and abdomen were examined grossly. Microscopically, sections of lung, liver, spleen, and kidney were studied in each animal. In Experiments 4 and 5, the various muscles of the affected leg were examined grossly and microscopically. In both the gross and microscopic examination evidence of disease peculiar to rabbits, specifically coccidioidomycosis, was found in many of the animals. For this reason only findings bearing a direct relationship to amniotic fluid embolism were recorded.

Amniotic fluid used in the experiments was obtained from human beings at the time of elective cesarean section. Only that of patients with unruptured membranes was used in order to avoid bacterial contamination. The fluid was aspirated with a syringe immediately after the uterus was opened and a small opening in the amniotic sac had been made. It was then placed in a sterile vial and refrigerated until use.

The meconium was aspirated from the rectum of newborn fetuses, diluted up to five times its volume with sterile physiological saline, placed in sterile vials, and then refrigerated until use. For intravenous administration of the material, the marginal vein of the ear was used and for arterial injection the femoral artery was exposed surgically and utilized.

The experiments were carried out in the following sequence:

Experiment 1: Amniotic fluid injection into the marginal vein of the rabbit ear
Experiment 2: Injection of amniotic fluid rich in vernix caseosa into the marginal vein of the rabbit ear
Experiment 3: Dilute meconium injection into the marginal vein of the rabbit ear
Experiment 4: Injection of amniotic fluid rich in vernix caseosa into the femoral artery of the rabbit
Experiment 5: Dilute meconium injection into the femoral artery of the rabbit
Experiment 6: Injection of amniotic fluid rich in vernix caseosa into the marginal ear vein of an anesthetized rabbit
Experiment 7: Dilute meconium injection into the marginal ear vein of an anesthetized rabbit

Results

The procedure, observations, and pathological findings of the experiments are summarized in Table I. Injection of amniotic fluid containing little vernix into the venous system produced no clinical effect and when sacrificed after 48 hours the animals showed only minimal changes in the pulmonary arterioles and capillaries. In Experiments 2 and 6 amniotic fluid rich in vernix was injected into the venous system of the rabbit. Each animal exhibited a typical picture of particulate matter embolism. At autopsy lanugo, vernix, and squamae were present in considerable quantities in the pulmonary arterioles and capillaries. Nembutal anesthesia used in Experiment 6 offered no protection to the animals. Lack of neutrophilic response in the pulmonary emboli may be attributed to the short survival times of the rabbits.

Experiments 3 and 7 produced identical results with Experiments 2 and 6 except that at autopsy meconium embolism rather than amniotic fluid embolism was the main pathological finding within the pulmonary vessels.

In Experiment 4 a quantity of amniotic fluid rich in vernix equal to a fatal intravenous dose was injected into the femoral artery of an anesthetized rabbit. No apparent changes were seen in the animal and when sacrificed in 24 hours the pulmonary tissues showed no embolism. The muscles of the injected leg showed "splinter hemorrhages" and the arterioles of the leg showed thromboses and perivascular neutrophilic infiltration.

Experiment 5 consisted of injecting an amount of meconium suspension equal to the lethal intravenous dose into the femoral artery of an anesthetized animal. These animals showed no clinical effect from the injection and when sacrificed 48 hours later showed absence of emboli in the pulmonary vessels. The leg muscles of the injected side exhibited meconium embolus of the femoral artery with neutrophilic invasion of the embolus.

TABLE I. PROCEDURE, RESULTS, AND PATHOLOGICAL FINDINGS OF EXPERIMENTS

INJECTION	AVERAGE SURVIVAL TIME AND SYMPTOMS	PATHOLOGY
1. 20 c.c. amniotic fluid with little vernix injected into marginal ear vein in 10 minutes. No anesthesia	Asymptomatic Sacrificed in 48 hours	Occasional squamae in pulmonary arterioles and capillaries
2. 20 c.c. amniotic fluid rich in vernix into marginal ear vein injected in 5 minutes. No anesthesia	17 minutes, 45 seconds Restlessness, dyspnea, convulsions	Petechiae of thymus and pericardium. Massive pulmonary embolism with squamae and meconium. No neutrophilic response
3. 4 c.c. of a 1 to 4 meconium suspension in saline injected into the marginal ear vein in 1 minute. No anesthesia	2 minutes, 50 seconds Dyspnea, restlessness, convulsions, coma	Massive meconium embolism in right ventricle and pulmonary vessels. Occasionally squamae seen in arterioles. Slight neutrophilic response in vessels
4. 20 c.c. of amniotic fluid rich in vernix into femoral artery injected in 5 minutes. Intravenous Nembutal anesthesia	Asymptomatic Sacrificed in 48 hours	No lung changes. "Splinter hemorrhages" in leg muscles. Thromboses of injected leg with marked neutrophilic reaction in and around these vessels
5. 4 c.c. of 1 to 4 meconium suspension in saline into femoral artery injected in 1 minute. Intravenous Nembutal anesthesia	Asymptomatic Sacrificed in 48 hours	No lung changes. "Splinter hemorrhages" in muscle of injected leg. Meconium embolus in vessels of this leg with thromboses and many neutrophiles in vessels
6. 20 c.c. amniotic fluid rich in vernix into marginal ear vein injected in 5 minutes. Intravenous Nembutal anesthesia	2 minutes, 5 seconds Dyspnea, rapid and shallow respirations	Petechiae of thymus and pericardium. Massive pulmonary embolism with squamae and granular debris. No neutrophilic invasion
7. 4 c.c. of 1 to 4 meconium suspension in saline into marginal ear vein injected in 1 minute. Intravenous Nembutal anesthesia	1 minute, 30 seconds Dyspnea, tremors	Petechiae of thymus, spleen, and pericardium. Massive meconium embolism of pulmonary arterioles. Occasional squamae and lanugo seen in vessels. No neutrophilic response

Comment

Although previous writers[6, 10, 27, 28] contend that amniotic fluid pulmonary embolism is fatal by virtue of an "anaphylactoid reaction," the preceding experiments conclusively prove that death is rather a result of the mechanical blocking of the pulmonary vessels by particulate matter. If death were a result of an "anaphylactoid reaction" then intra-arteriole administration of the material should have produced death equally as fast as the intravenous administration. However, the animals survived intra-arteriole injection of amniotic fluid and its particulate matter because the vascular bed of the injected extremity filtered out the particulate matter, thereby sparing the lung from embolic disorder.

A clinical observation offers another point to disprove the anaphylactic shock theory. Frequently at cesarean section the peritoneal cavity is contam-

inated with a considerable quantity of amniotic fluid, vernix, and meconium. This occurs without any apparent ill effect. The peritoneum, however, is a body surface which has remarkable power of absorption. Air, ascitic fluid, blood, and many other substances are efficiently taken up by it. It is only logical to suppose that the peritoneum would also absorb the amniotic fluid released at the time of cesarean section. If this is true, anaphylactic shock should be the consequence.

The finding of only a small amount of particulate matter on microscopic section from fatal cases in human beings has been used as an argument against the theory that embolism itself causes death. It must be remembered, however, that the tissue on a given microscopic slide represents only a minute quantity when compared to the tissue of an entire lung. Thus a minimal change on a particular section of tissue when multiplied to incorporate the tissue of both lungs would make this minimal change a massive process with countless vessels involved.

Summary

1. A case report of fatal pulmonary amniotic fluid embolism is presented.

2. Amniotic fluid pulmonary embolism was reproduced experimentally in rabbits and the clinical and pathological findings were similar to those found in human beings.

3. Pulmonary embolism rather than anaphylactic shock is productive of death in amniotic fluid pulmonary embolism.

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BIOCHEMICAL AND HISTOCHEMICAL ALKALINE GLYCEROPHOSPHATASE IN NORMAL ENDOMETRIUM, ENDOMETRIAL HYPERPLASIA, AND ADENOCARCINOMA*

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HISTOCHEMICAL studies by the Gomori technique on alcohol-fixed tissue for endometrial alkaline phosphatase during the human menstrual cycle have been reported by several authors.[1, 2, 3] It has been found that marked variations in the enzyme activity occurred during the menstrual cycle. The activity, high during the proliferative phase, is reduced during the secretory phase, and disappears several days before menstruation.

In view of these findings, the present study was undertaken to assay quantitatively this variation in the normal cycle and in certain abnormal states, and to reinvestigate the histochemical findings, using a fresh frozen tissue technique.[8]

Method

The method employed for the biochemical assay was that of Bodansky.[4] This consists of adding 1 c.c. of 5 per cent homogenate to 10 c.c. of 0.05 per cent sodium glycerophosphate in 0.42 per cent monosodium diethylbarbiturate buffer. The mixture is incubated for 1 hour at 37° C. The pH of this solution is 8.6. The enzyme is then inactivated by the addition of 9 ml. of 20 per cent trichloracetic acid and the mixture centrifuged. Inorganic phosphate is determined by the Fiske and Subbarow method.[5] The phosphate is also determined in the homogenate and substrate and subtracted from the experimental values. The values are expressed in gammas of inorganic phosphorus liberated per milligram of wet weight of tissue.

The endometrial specimens were obtained by curettage and kept frozen until the assay was done. Portions of each specimen were fixed in 95 per cent ethanol for histological and histochemical examination and selected specimens were frozen in isopentane cooled by liquid nitrogen for histochemical study by an alternate technique. The histological sections were studied to eliminate abnormal cases and dated, using the technique described by Noyes, Hertig, and Rock.[6] The histochemical assays of phosphate liberation were done by the Gomori technique[7] for paraffin sections and in selected cases by a fresh frozen section technique described elsewhere.[8]

Results

Forty-one of the cases studied seemed to have normal cycles. The quantitative biochemical results have been summarized in the accompanying bar graph (Fig. 1). These biochemical data in general confirm the impression

*Aided by a grant from the Maryland Division of the American Cancer Society to R. W. Te Linde and Howard W. Jones, Jr., and by a grant from the S. & N. Katz Foundation.

from previously reported histochemical studies. However, some activity was found in all specimens, even in the postmenstrual and premenstrual phases. Since the histochemical sections revealed activity only in the blood vessels, at these times, it may be inferred that the principal activity is derived from these structures. The highest values were found in the 14 to 18 day period, which showed an increase of 200 per cent over the 1 to 8 day period; in the premenstrual phase there was a decrease to about the postmenstrual level.

Five cases of endometrial hyperplasia were studied and showed activity comparable to that of the proliferative phase of the normal cycle. The values obtained were 3.8, 2.8, 2.1, 2.0, and 4.4 gammas per milligram. Also, three cases of adenocarcinoma were relatively active with values of 1.6, 1.8, and 2.6 gammas per milligram. However, in one case of unruptured ectopic pregnancy the decidua showed only 0.7 gamma per milligram and no activity histochemically.

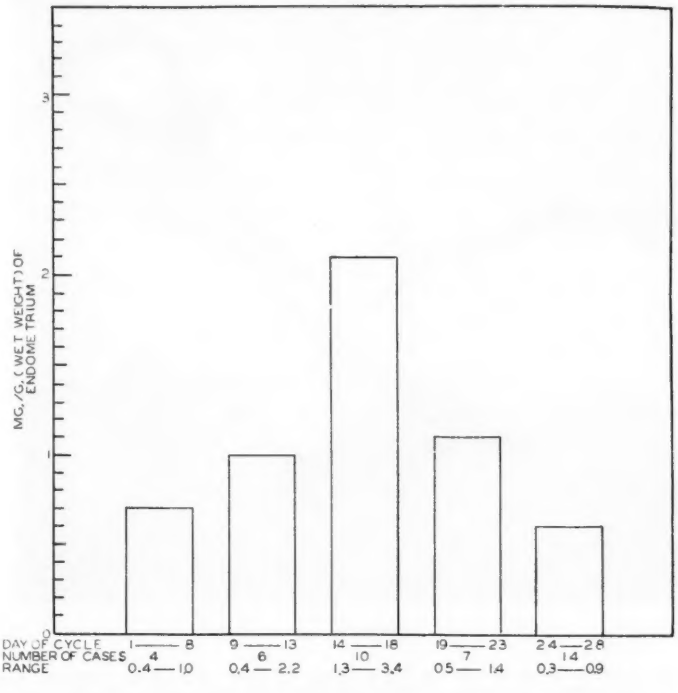

Fig. 1.—Phosphate release, measured in milligrams per gram of endometrium, during the human menstrual cycle, using glycerophosphate as substrate.

The results of histochemical studies using sections of fresh frozen tissue confirmed in general the results reported by others using the standard alcohol-fixation, paraffin-embedded material with important differences in detail. Our material of the former type revealed an absence of activity in the stroma in any phase of the cycle even immediately adjacent to very active gland cytoplasm. One may take the view that stromal nuclear activity in juxtaposition to active gland cytoplasm in the standard Gomori procedure is due to diffusion. Similarly, lesser activity in the glandular nuclei of frozen material may suggest a similar view. With these differences, the frozen material confirms other work which reports high activity in the endometrial blood vessels throughout the cycle, increasing activity in gland cytoplasm in the proliferative phase (Fig. 2), reaching its greatest intensity at about day 18 and

disappearing from the gland cytoplasm a few days before menstruation (Fig. 3). Gland nuclei exhibit some activity but much less than with the alcohol-fixed material.

Fig. 2.

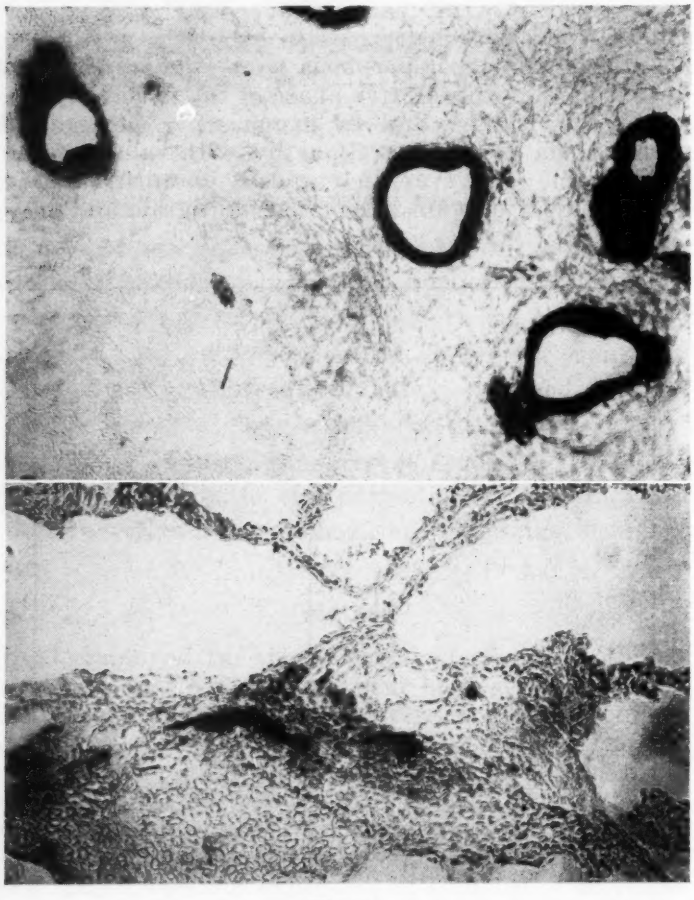

Fig. 3.

Fig. 2.—Fresh frozen section of endometrium of day 12 of a normal mentrual cycle, showing alkaline phosphatase activity. Note absence of stromal activity even immediately adjacent to very active glands. Incubation four hours at pH 9.

Fig. 3.—Fresh frozen section of endometrium of day 26 of a normal menstrual cycle, showing alkaline phosphatase activity. Except for the blood vessels this section is almost completely negative. It is almost invisible under the microscope and a photomicrograph is possible only by using a suitable filter. Incubation four hours at pH 9.

Comment

The significance of alkaline glycerophosphatase in the metabolism of the endometrium is unknown. However, the cyclic variation in its activity is a constant physiological observation, apparently correlated with ovarian steroid activity. The quantitative assay of its activity may serve as a measure of physiological competence of the endometrium on a particular cycle day. The histochemical assay serves to localize the variable activity in the cytoplasm of the gland cells.

Summary and Conclusions

1. Phosphate released from glycerophosphate at pH 8.6 is relatively low at the beginning of the normal menstrual cycle but rises to a maximum of about 2 mg. of phosphorus per gram of endometrium after one hour's incubation at midcycle, and then falls off before the onset of menstruation.

2. Histochemical observations indicate that the blood vessels appear equally active throughout the cycle and the stroma exhibits no activity. The cyclic variation is apparently due to variations in the activity of the enzyme in the cytoplasm of the gland cells.

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THE TRANSMISSION OF MEPERIDINE ACROSS THE HUMAN PLACENTA*

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QUANTITATIVE data on the transmission of certain anesthetic and analgesic drugs from the maternal to the fetal circulation have been cited.[1-3] Such information is of value to the obstetrician and anesthesiologist for a better understanding of the effects upon the the newborn baby of drugs administered to the mother during labor.

Hitherto, such knowledge was unavailable with regard to meperidine (Demerol). This drug has been used with increasing frequency for the relief of labor pain because it is said to produce little or no effect upon the respiration of the newborn baby when employed in this manner.[4] Because of the important place meperidine has in the management of labor, the current studies of the pattern of its placental transfer from mother to fetus were undertaken.

Methods

Nine healthy pregnant women at term were used for this study. Two patients were delivered by cesarean section, the remainder spontaneously, with episiotomy. Meperidine in doses of 50 to 100 mg. was administered intramuscularly or intravenously during labor. The average total quantity of drug per patient during labor was 175 mg. and ranged from 50 to 300 mg. The last dose of meperidine varied from 40 minutes to 3 hours and 38 minutes prior to delivery. The first dose varied from 1 hour and 40 minutes to 15 hours before delivery. The method of drug administration was adjusted to the need of the patient for satisfactory analgesia.

Five patients were anesthetized for delivery with nitrous oxide-oxygen (a minimum concentration of 25 per cent oxygen was given); two with cyclopropane, and one each with low spinal anesthesia and caudal block.

At delivery, samples of blood were drawn simultaneously from the mother and the umbilical cord. The latter was considered representative of the fetal blood. Meperidine in plasma was determined according to a method to be published elsewhere.[5] This method has been shown to be specific in that it included none of the metabolites of meperidine in the measurement.

Results

Plasma levels of meperidine indicate clearly that the drug crossed the placenta in significant concentrations (Table I). These varied from 45 to 106

*Supported in part by the Squibb Institute for Medical Research.

TABLE I

PATIENT	TYPE OF DELIVERY	MEPERIDINE (IN MG.)	ROUTE OF ADMINISTRATION	TIME PRIOR TO DELIVERY (IN HR. AND MIN.)	ANALGESIC EFFECT ON MOTHER	DEPRESSANT EFFECT ON INFANT	ANESTHESIA	MATERNAL PLASMA LEVEL (IN MG./L.)	CORD BLOOD LEVEL (IN MG./L.)
He	Vaginal	100	IM	2:00	Good	0	Cyclopropane	0.40	0.22
Zi	Cesarean	50	IM	1:43	Good	0	Cyclopropane	0.38	0.24
Po	Vaginal	50	IM	2:40	Good	0	Nitrous oxide	0.29	0.13
		50	IM	1:15					
Fr	Vaginal	100	IM	1:40	Good	Moderate depression	Nitrous oxide	0.45	0.38
Ni	Vaginal	75	IM	4:08	Poor	0	Nitrous oxide	0.50	0.39
		75	IM	2:00					
		50	IV	0:43					
St	Vaginal	100	IM	7:00	Good	0	Nitrous oxide	0.76	0.55
		100	IM	4:00					
		100	IV	2:45					
Pa	Cesarean	100	IM	15:00	Good	0*	Low spinal	0.73	0.76
		100	IM	9:00					
		50	IV	0:40					
Bu	Vaginal	100	IM	4:52	Good	0†	Nitrous oxide	0.23	0.26
		100	IM	3:38					
Al	Vaginal	100	IM	15:00	Good	0	Caudal	1.02	0.72
		50	IM	11:00					
		50	IM	6:40					
		50	IM	3:15					

*Spontaneous breathing early. Aspirated meconium. No sequelae.
†Difficult to evaluate. Delivery was complicated by impaction of the shoulders of the fetus in the birth canal. A difficult delivery was followed by fetal anoxia requiring 20 minutes of intratracheal oxygen insufflation. Fetal recovery was satisfactory.

per cent (average 77 per cent) of the levels measured simultaneously in the maternal blood.

Satisfactory analgesia for the mother was achieved in all but one patient. In only one instance was there a clearly demonstrable depression of fetal respiration, presumably due to meperidine. Even so, the fetal plasma level of 0.38 mg. per liter was not the highest encountered. There were two other complications in the newborn. One was attributable to early intrauterine respiration and aspiration of meconium; the other to a difficult delivery caused by shoulder impaction of the fetus. Neither complication was harmful to the baby.

Comment

With the aid of a sensitive method for its estimation, it was demonstrated that meperidine enters the fetal circulation relatively freely after parenteral administration to the mother. It also appears that doses of the drug which can produce satisfactory analgesia in the mother do not necessarily cause significant depression of respiration in the newborn baby. The rate of transplacental movement of the drug is unknown.

Summary

1. Meperidine crosses the human placenta in significant concentrations.

2. In therapeutic doses administered to the mother, meperidine appears to cause little or no depression of respiration of the newborn child.

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COLLECTION OF PLACENTAL BLOOD*

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THE thought of possible utilization of placental blood may have occurred to the first obstetrician. Rubin[1] in 1914 was probably the first to describe the use of placental blood for transfusions. Since then, many investigators have recorded their experiences with the collection, storage, and use of placental blood for transfusions. Many of these workers have reported successful results.[2-5] Others have found a high percentage of bacterial contamination of the placental blood accompanied by a high incidence of transfusion reactions.[6]

In the light of present-day knowledge of transfusion of stored blood, it is apparent that two defects stand out in the techniques employed by the past investigators: (1) Rh factor determinations were not made; (2) the technique of blood collection was subject to contamination.

I have experimentally adapted the modern method of blood collection used in maintaining blood banks to the collection of placental blood. Undoubtedly the technique described has been used by others although no reference has been found in the literature to date. While I cannot as yet publish blood culture studies, it is hoped that this preliminary report describing the technique of collection of placental blood may arouse interest in the subject in other investigators. The desirability of a source of blood or blood products other than that of adults seems apparent for the national welfare.

Technique

The apparatus consists of a metal stand and ring holder, a large funnel to hold the placenta, 2 hemostats, Transfuso Vac bottle (150 c.c.),† Plexitron 2 needle blood collection set, sterile.

The placenta is placed in the funnel, fetal surface down. Then the clamped end of the umbilical cord is inserted through the funnel opening and the end of the cord seized and clamped with a hemostat. The first clamp on the cord is then removed and the umbilical cord drawn downward through the funnel opening (Fig. 1). The funnel containing the placenta is then placed in the ring holder. The tubing of the blood collection needle is clamped by a hemostat and the sterile needle is inserted into the Transfuso Vac bottle which is then suspended on a hook adjacent to the funnel.

The umbilical cord is then carefully cleaned, first with dry gauze and then with several alcohol sponges. The needle at the other end of the blood collection tube is then inserted into the umbilical vein just above the hemostat.

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*Presented before the Chicago Gynecological Society, March 21, 1952.

†Transfuso Vac, 150 c.c. bottle, Model H-4, and Plexitron 2 needle blood collection set, Model R20, sterile, were generously supplied by the Baxter Laboratories, Inc., Morton Grove, Ill.

The clamp on the blood collection tube is then loosened and the blood is allowed to flow slowly into the vacuum bottle. The umbilical cord is milked gently downward during the process. No pressure is made on the placenta. When the placenta is exsanguinated, the clamp is replaced on the tube and the needle removed from the bottle and then from the cord.

The bottle of blood is then marked with suitable identification and placed in the refrigerator. The blood remaining in the collection tube may be used for the pilot tube or may be aspirated through cotton into the bottle before the needle is removed from the bottle. This adds approximately 10 to 15 c.c. to the total volume of blood in the bottle. Approximately 5 to 10 c.c. of residual blood can be obtained from the cord or placental vessels after termination of the exsanguination.

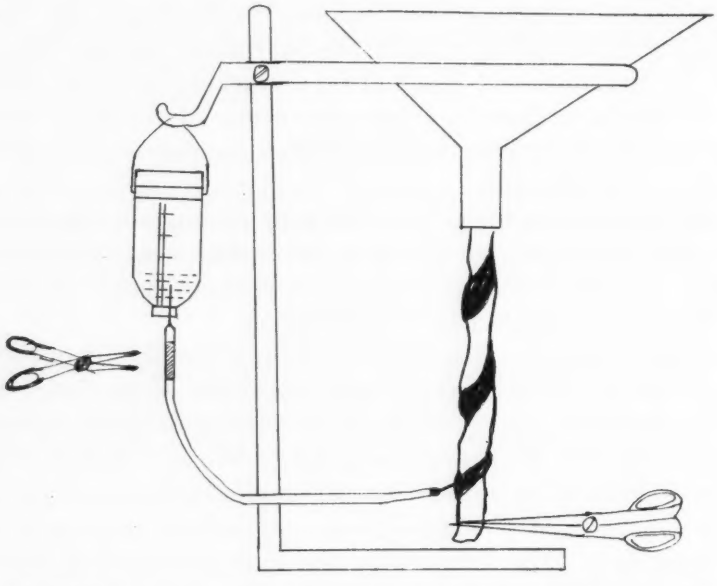

Fig. 1.—Diagram of apparatus and technique for placental blood collection. Placenta is in funnel holder. Clamp is on end of umbilical cord. The clamp on the left is removed from tubing after needle is inserted into umbilical vein. This clamp is replaced on tubing after placenta is exsanguinated. Needle is then removed from bottle.

Special Considerations

1. The exsanguination of the placenta must be performed immediately after delivery. Aside from possible changes in the blood, cold placentas or placentas stored in the refrigerator yield consistently a low quantity of blood. Examination of placentas stored as long as 10 days in the refrigerator reveals no coagulation of the blood but it is too viscous for aspiration. Immediate exsanguination yields on the average 100 c.c. of placental blood.

2. Method of delivery of placenta: It is superfluous to state at the outset that there should be no interference with the obstetrician's delivery and examination of the placenta. One may suggest the desirability of obtaining an intact placenta. If the obstetrician believes, as Smith[7] does, that it is immaterial to the baby whether the umbilical cord is clamped early or late, one may request an immediate clamping of the cord after delivery of the baby. The volume of placental blood is greater when the cord is clamped early but this finding is not consistent.

The umbilical cord should be clamped as close to the baby as is practical in order to leave a long column of blood in the cord attached to the placenta. This should not arouse any objection from the obstetrician. The cord clamp should not be removed except by the investigator. Immediately after inspection of the placenta by the obstetrician, it should be appropriated by the investigator who will perform the exsanguination in a separate room containing the equipment.

3. Volume of placental blood: The volume of blood obtained by exsanguination of a placenta varies from 40 c.c. to 150 c.c. It is desirable to avoid wasting material and time on placentas which yield less than 80 c.c. of blood. The following criteria are helpful in deciding whether to apply aspiration or not: (a) Large placentas yield a larger quantity of blood than small placentas. (b) Early clamping of the cord results in a larger blood volume but this is not invariable. (c) Long cords yield a larger volume of blood. (d) Cords which have a turgidity and distention of their vessels yield consistently large quantities of blood.

In other words, small placentas with short flaccid cords are unsuitable for use.

There is always some residual blood in the cord and placental vessels which, as previously stated, may be used for pilot studies. Familiarity and practice with the technique results in uniform quantity of blood. Because of the distribution of the time of deliveries in a 24 hour period, a single investigator can utilize only approximately one-third or one-half of the number of placentas of a delivery service. A few placentas are lost to the investigator if the cord clamp is advertently opened, allowing the cord to drain. The torn placenta cannot be used.

Though the extent of the physiologic increase in the number of erythrocytes of the cord blood is variable, the use of 40 c.c. of A.C.D. solution in the Transfuso Vac bottle does not reduce the hematocrit reading below 44 per cent where the volume of blood is 100 c.c. It may be preferable to use only 20 c.c. of anticoagulant solution. One hundred placentas should yield 10 L. of blood with a high biologic value. Placental blood is probably free of the virus causing hepatitis.

While pilot tube studies are representative of the bottled blood, it is desirable to have pertinent data on the mother, particularly the serologic reports.

Summary

A method of collecting placental blood is described. The technique is similar to that employed in blood donor centers. Other considerations involving the availability of placentas and use for placental blood are discussed. The purpose of this report is to interest other investigators in the experimental use of placental blood.

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THE MIDPLANE BIISCHIAL DIAMETER

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IN PREVIOUS communications attention was called to the desirability of measuring the width of the lower midpelvis anterior to the bases of the ischial spines.[1, 2] Experience which has accumulated since then points even more strongly to the significance of this diameter, particularly with reference to the narrow upper midpelvis, and high occipitoposterior arrests.

The Midplane Biischial and the Outlet Biischial Diameters

The diameter between the bases of the ischial spines was originally named the "interischial" diameter,[1] to differentiate it from the "biischial" or transverse diameter of the outlet. These midplane and outlet diameters will now be designated more descriptively as the "midplane biischial," and the "outlet biischial" diameters, respectively.

There is considerable individual variation between these two diameters, to the extent that the width of one cannot be estimated if the width of the other is known.[1] Furthermore, there is no accurate method for the measurement of the outlet biischial diameter.

The Narrow Midplane Biischial and the Narrow Bispinous Diameters

There is likewise a marked individual variation between the midplane biischial and the bispinous diameters. Thus, in a consecutive series of 151 private cases in which the bispinous diameter was 9.5 cm. or less, the average value for the midplane biischial was found to be 10.26 cm. The average difference between the midplane biischial and the bispinous diameters was 1.12 cm. This difference was 0.3 cm. or less in 2 per cent of the cases, and 1 cm. or more in 73 per cent of the cases. These individual and average differences are considerably greater than those which were obtained in an unrestricted sample of 384 cases previously reported.[1] Here again, as in the case of the outlet biischial diameter, the midplane biischial cannot be estimated from measurements of the bispinous diameter, because of the considerable individual variation.

The width of the midplane biischial diameter, consequently, should be determined only by direct measurement. In actual practice this can readily be done, since it would be only a momentary incidental step in the measurement of the bispinous diameter by one of the roentgen methods,[3] or clinically by a method which was previously described.[1]

The Narrow Midplane Biischial Diameter

The average width of the midplane biischial diameter in the sample of 384 cases referred to, was 11.15 cm. For practical purposes, a midplane biischial diameter of 10.2 cm. or less, may be regarded as significantly contracted. There were 93 such cases in the present series of private cases, an incidence of 10.8 per cent.

The Narrow Upper Midpelvis and High Occipitoposterior Arrests

The midplane biischial diameter, taken together with the inlet transverse diameter, indicates the degree of convergence of the side walls of the pelvis. This makes possible a rough estimate of the width of the upper midpelvis.

The information thus obtained concerning the width of the upper midpelvis should be of value as a guide to the prevention and treatment of cases of high occipitoposterior arrest. This view is based on both direct and indirect evidence.[4, 5]

Material

The direct evidence consists of the following observations: In a series of 1,290 primiparas reported in 1936,[1] there were 12 cases of high occipitoposterior arrest in pelves with a narrow bispinous diameter. All of these cases were high midforceps deliveries, and 10 of them were very difficult and traumatic operations. Since then, in a series of over 2,000 primiparous deliveries, the incidence of high occipitoposterior arrest was reduced to less than one-half by the performance of cesarean section electively, or earlier in labor, in suspect cases. At the same time, high midforceps delivery for the posterior position in the transversely contracted upper midpelvis was almost entirely eliminated. This was accomplished with an increase in the incidence of cesarean section which was only slightly greater than the decrease in the incidence of high occipitoposterior arrests, and high midforceps delivery. In other words, the number of cesarean sections was not unduly increased in the effort to avoid difficult high midforceps deliveries.

Final conclusions cannot be drawn from the above observations, because of the paucity of the data, and because of the consideration that must be given to other factors. Tentatively, it may, however, be assumed that the improvement in the results noted was, in part, due to a better screening of cases which became possible because of the inclusion of the midplane biischial, the midplane sagittal, and the inlet transverse diameters in the study of the pelvis, as previously outlined.[2]

The Midplane Biischial Diameter and the Lower Anterior Pelvis

At the ischial spines, and below this level, the midplane biischial diameter may also be of clinical significance. At this level it is an important criterion of the capacity of the lower anterior pelvis,[2] through which delivery has been considered possible.[6, 7]

Summary

Attention is called to the midplane biischial diameter (the diameter between the bases of the ischial spines). A reduction in the width of this diameter to 10.2 cm., or less, is regarded as of clinical significance, with special reference to the narrow upper midpelvis, and high occipitoposterior arrests.

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ORAL TOLUIDINE BLUE* IN THE TREATMENT OF HYPERMENORRHEA

C. A. Lathrop, M.S., M.D., and W. T. Carlisle, B.S., M.D., Chicago, Ill.

ALLEN and associates have shown the presence of an unknown substance in the blood of some patients exhibiting abnormal bleeding which resembles heparin to the extent that it combines with the antiheparins toluidine blue and protamine sulfate.[1, 2] This group have also shown the efficacy of treating these patients with protamine sulfate and/or intravenous injections of toluidine blue.[3]

The present study was undertaken with two aims in view:

1. To determine the efficacy of toluidine blue taken orally in the treatment of hypermenorrhea.

2. To determine the feasibility of treating patients exhibiting hypermenorrhea with oral toluidine blue on a clinical basis only, that is, without the aid of a protamine titration,[4] to show definitely the presence or absence of the above-mentioned heparin-like substance.

The advantage of a preparation which may be taken in capsular form at home is obvious. It seems that, if this treatment is effective, it will be used primarily in private practice where a protamine titration would be too complicated and time consuming to be practical. Patients were therefore selected for treatment only on the basis of excessive menstrual bleeding in the absence of such obvious causes as uterine fibroids, ovarion tumors, etc. These patients, consequently, fall in that group which is often loosely termed functional uterine bleeding.

Method

The method used consisted of having the patients take one 100 mg. capsule of toluidine blue after meals three times daily, starting with the first day of menstruation and continuing as long as bleeding persisted. Dosage levels were arbitrarily taken far below the LD_{50} values as determined for mice, rats, and rabbits, by Haley and Stolarsky.[5]

Side reactions consisted of occasional nausea and burning on urination. These side reactions were in most cases insignificant, especially since these possibilities were always discussed with the patient and a warning given them that their urine would be blue. Side reactions increased when the dosage was increased from three to four capsules daily, some cases requiring the discontinuation of therapy.

Results

The results of therapy were reported by telephone daily and were scored as good, fair, or poor. A good result was deemed one in which menstrual flow was diminished to normal or less.

*Toluidine blue supplied by the Abbott Laboratories, Chicago, Ill.

Sixty-three patients were treated during an average of three menstrual periods. Forty-three patients reported good results, fifteen fair results, and five reported poor results. Two patients reporting good results with the first treatment reported relapses with subsequent treatments and were counted as showing poor results.

Comment

The good results of therapy as reported are probably too high. This may be attributed to (1) overzealous reporting of results, (2) psychic effect of therapy, (3) coincidental spontaneous improvement, and (4) a carefully selected group of patients.

Any such study which is based upon patient reporting of results must of necessity be discounted somewhat. It does appear evident, however, that in selected patients the use of oral toluidine blue is an effective treatment of hypermenorrhea.

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1. To determine the efficacy of toluidine blue taken orally in the treatment of hypermenorrhea.

2. To determine the feasibility of treating patients exhibiting hypermenorrhea with oral toluidine blue on a clinical basis only, that is, without the aid of a protamine titration,[4] to show definitely the presence or absence of the above-mentioned heparin-like substance.

The advantage of a preparation which may be taken in capsular form at home is obvious. It seems that, if this treatment is effective, it will be used primarily in private practice where a protamine titration would be too complicated and time consuming to be practical. Patients were therefore selected for treatment only on the basis of excessive menstrual bleeding in the absence of such obvious causes as uterine fibroids, ovarion tumors, etc. These patients, consequently, fall in that group which is often loosely termed functional uterine bleeding.

Method

The method used consisted of having the patients take one 100 mg. capsule of toluidine blue after meals three times daily, starting with the first day of menstruation and continuing as long as bleeding persisted. Dosage levels were arbitrarily taken far below the LD_{50} values as determined for mice, rats, and rabbits, by Haley and Stolarsky.[5]

Side reactions consisted of occasional nausea and burning on urination. These side reactions were in most cases insignificant, especially since these possibilities were always discussed with the patient and a warning given them that their urine would be blue. Side reactions increased when the dosage was increased from three to four capsules daily, some cases requiring the discontinuation of therapy.

Results

The results of therapy were reported by telephone daily and were scored as good, fair, or poor. A good result was deemed one in which menstrual flow was diminished to normal or less.

*Toluidine blue supplied by the Abbott Laboratories, Chicago, Ill.

Sixty-three patients were treated during an average of three menstrual periods. Forty-three patients reported good results, fifteen fair results, and five reported poor results. Two patients reporting good results with the first treatment reported relapses with subsequent treatments and were counted as showing poor results.

Comment

The good results of therapy as reported are probably too high. This may be attributed to (1) overzealous reporting of results, (2) psychic effect of therapy, (3) coincidental spontaneous improvement, and (4) a carefully selected group of patients.

Any such study which is based upon patient reporting of results must of necessity be discounted somewhat. It does appear evident, however, that in selected patients the use of oral toluidine blue is an effective treatment of hypermenorrhea.

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Department of Case Reports New Instruments, Etc.

TRANSPARENT MANIKIN FOR THE TEACHING OF OBSTETRICS*

RUTH C. WAKERLIN, CHICAGO, ILL., AND FRANK E. WHITACRE, M.D., MEMPHIS, TENN.

(From the Illustration Studios, University of Illinois College of Medicine, Chicago, and the Department of Obstetrics and Gynecology, University of Tennessee College of Medicine, Memphis)

MEDICAL teaching models in the past have been constructed of many varieties of materials, most notable among which are wax, plastic, wood, and rubber. While these materials are still widely used, in recent years several new substances have been introduced which widen the possibilities for the model maker. For example, the development of synthetic resins (plastics) which are transparent, easily molded, and easily fabricated has made transparent teaching models possible. Such models have the advantage of making internal structures visible with relation to external form.

Inspired by earlier German figures, but working independently, the staff of the Illustration Studios of the University of Illinois completed in 1947 a greater than life-sized transparent model of a pregnant woman (Fig. 1). This model has since formed the central display piece in the University of Illinois exhibit, "The Miracle of Growth," in the Museum of Science and Industry of Chicago. It is modeled in the full round at term pregnancy with pelvis, fetus, and uterus visible inside the figure.

It was this transparent pregnant figure which in 1947 inspired the present work on transparent obstetrical manikins. It is perhaps also of interest that the fabrication techniques finally adopted for the manikins were those originally developed in order to build the pregnant figure.

Advantages of a Transparent Obstetric Manikin

The most frequent and by far the most important operation of delivery is the use of forceps. In teaching the techniques of forceps delivery, the transparent manikin is of great value. It allows students to see clearly maneuvers which help to prevent injury to both mother and child. Our purpose is not to demonstrate any particular manipulation or operation but to present and demonstrate transparent manikins for the teaching of obstetrics.

Sellheim recognized the value of models for teaching obstetrics but did not have the advantage of the transparent materials now available. In the past, students depended upon their own interpretation of what they read or heard or upon drawings and opaque models. When transparent models are added to this list, obstetric teaching at last is made more graphic than was ever dreamed possible. The tools are available by means of which the student may see for himself the anatomical relationships and understand the techniques employed in the practice of obstetrics to protect both fetal and maternal life.

Of particular note in the development of models for obstetrical teaching in this country are Dickinson and Belskie working in New York, and Falls and Holt in Chicago. Dickinson[1] in an early published work brought out the value of obstetric teaching by means of charts and models and again pointed out, by example, what can be done by the application of sculpture[2] to practical teaching in obstetrics. Barnes[3] emphasized the obstetric teaching value of the Dickinson-Belskie sculptured models.

The greatest contribution of visual teaching in obstetrics is to make visible to students the normal mechanism of labor. In normal labor this mechanism is usually self-

*Presented before the Memphis Obstetrical and Gynecological Society, Nov. 30, 1951, and the Fifth American Congress on Obstetrics and Gynecology at Cincinnati, March 31 through April 4, 1952.

sufficient, but in abnormal labors assistance must be given. If the student can see what he should do, he will understand how to carry it out. In fact, it is essential that students of obstetrics understand the normal mechanism of labor since successful manipulative and operative procedures using the vaginal route merely carry out what nature has failed to accomplish.

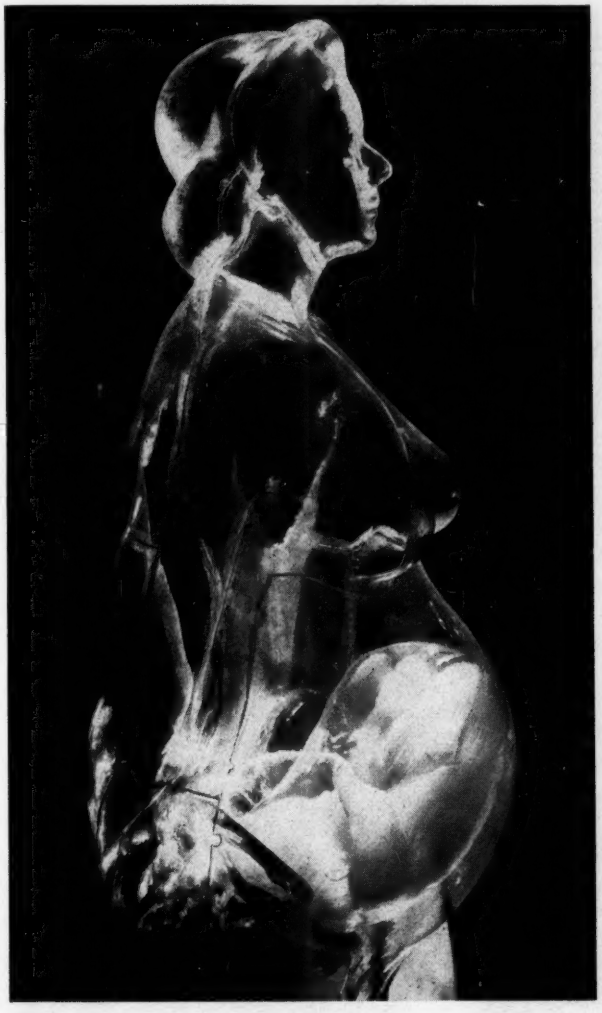

Fig. 1.

Construction and Presentation of Transparent Obstetric Manikins

The present study was begun late in 1947 under the joint sponsorship of the Children's Bureau through the Tennessee Public Health Division, the University of Illinois College of Medicine, and University of Tennessee College of Medicine.

In this study two methods of fabrication have been tried.

Solid Casting Technique.—A solid transparent manikin was cast of liquid plastic using Selectron-type resins (supplied by courtesy of the Castolite Company. This fabrication technique, however (because of the large size of the casting), proved too difficult and uncertain to be practical. In addition, lens effects produced by the curved surfaces of the finished castings make visibility poor.

Shell Mold Technique.—The two double-walled shell manikins shown (Figs. 2, 3, 4, and 5) were formed from sheets of transparent plastic (Plexiglas or Lucite) using the same

vacuum molding techniques as were used for the model of the pregnant woman. The resulting manikins have the advantage of complete visibility and relative ease and economy of fabrication.

Fig. 2.

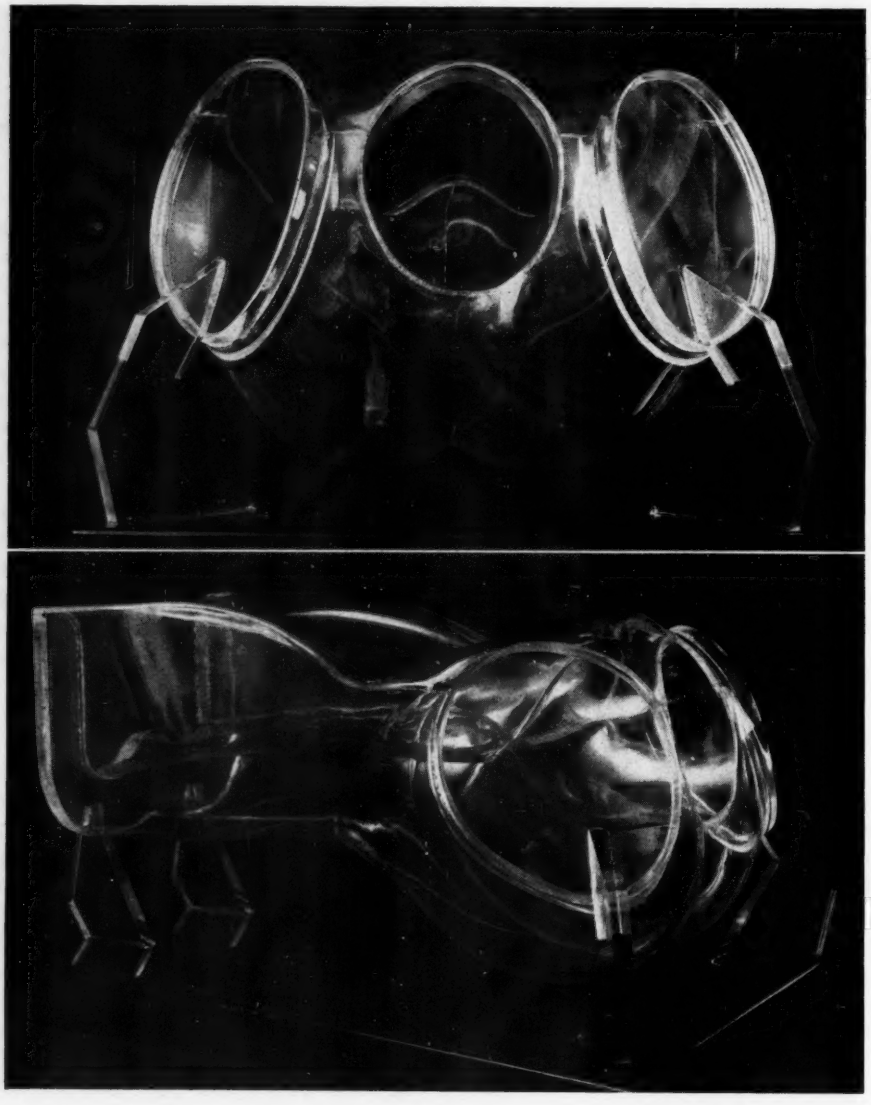

Fig. 3.

We are presenting two transparent shell manikins:

1. The first one attempted is a replica of an older wooden manikin, from which the molds were taken. This was constructed of six sheets of plastic which were formed, trimmed, and cemented together (Figs. 2 and 3). Two of these manikins have been produced and one has been in use for a period of months in the Department of Obstetrics and Gynecology at the University of Tennessee for the demonstration of operative and manipulative obstetrics.

2. The second is a revision of the transparent manikin above incorporating changes in the birth canal and several other structural modifications and teaching refinements (Figs. 4 and 5). These modifications are as follows:

a. Improvement in the shape of the birth canal, inlet, midplane, and outlet.

b. Inclusion of a plastic cast of the bony pelvis inside the walls of the manikin making

it possible to identify bony landmarks. The pelvis which was used as a model is a near-normal European female pelvis obtained in 1935 in Berlin, from Dr. Robert Meyer.

A specially prepared actual fetus may be used with considerable success in demonstrating obstetric techniques on the transparent manikins. Experiments have also been conducted on the development of a flexible plastic fetus. The results are not yet completely satisfactory but give promise of very successful further development.

Fig. 4.

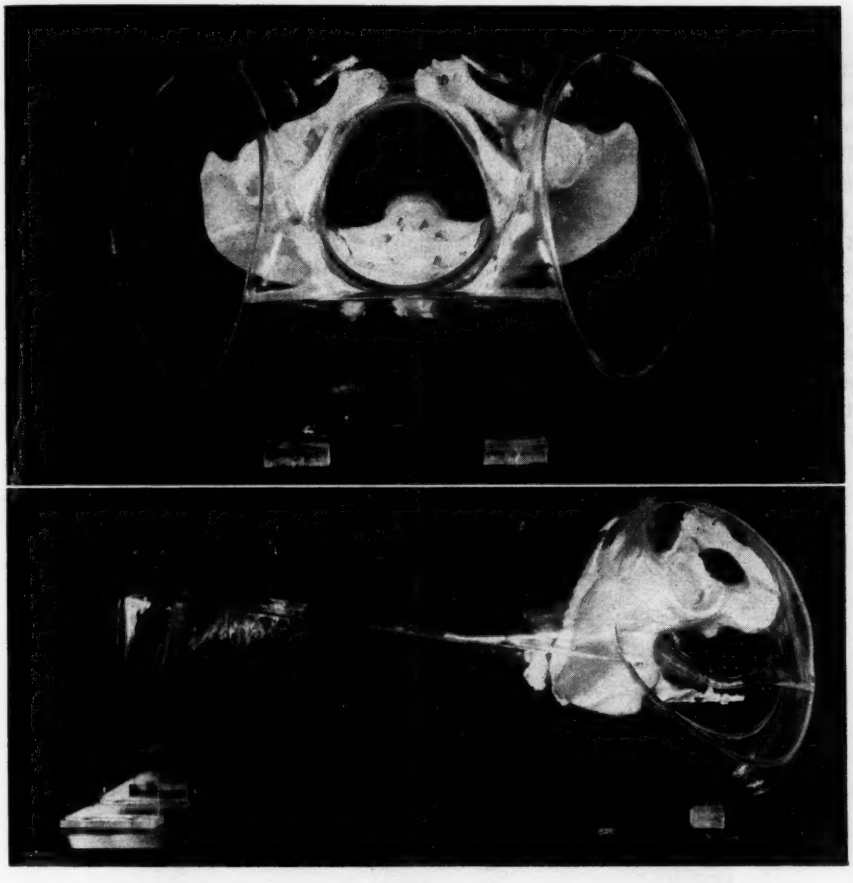

Fig. 5.

It has been demonstrated that transparent obstetrical manikins have a special value in teaching the mechanism of normal labor and the techniques of operative obstetrics. In addition, this study has shown that production of transparent manikins on a wider scale is now possible.* It is probable that further refinements will be incorporated into the present design for the manikins in order to make them more useful and effective as teaching media.

Vincent P. Destro had much to do with the construction of the first models and the reproduction of the bony pelvis.

Dr. James B. McCormick modified the earlier models to be more anatomically correct.

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*Those interested in securing such models should communicate with Dr. James B. McCormick of the Histoslide Company, Grant Place, Chicago.

PSEUDOMUCINOUS CYSTADENOCARCINOMA OF THE OVARY

A. W. Strauss, M.D., and A. W. Strauss, Jr., M.D., Little Rock, Ark.

(From the University Hospital)

PSEUDOMUCINOUS cystadenocarcinoma of the ovary is a rare entity in comparison with other ovarian tumors. At the University of Arkansas School of Medicine less than one case per year during the past ten years has gone through their clinics.

The case which is reported here is of a 54-year-old Negro patient who first developed symptoms in 1944. Surgery was performed at that time. She stated that a cyst the size of an orange was removed from the left ovary, and that it contained a jellylike material. During surgery the cyst was inadvertently ruptured. Unfortunately, the hospital in which she was confined had no pathology department and microscopic examination was not made.

In 1948 the patient entered the University Hospital where she again underwent surgery. The abdomen was greatly distended by gelatinous material. Microscopic sections showed the tumor to be papillary pseudomucinous cystadenocarcinoma of the ovary with metastases to the peritoneum. About 6,000 c.c. of gelatinous material were evacuated from the abdomen. X-ray therapy was attempted but was discontinued because of an aggravation of symptoms.

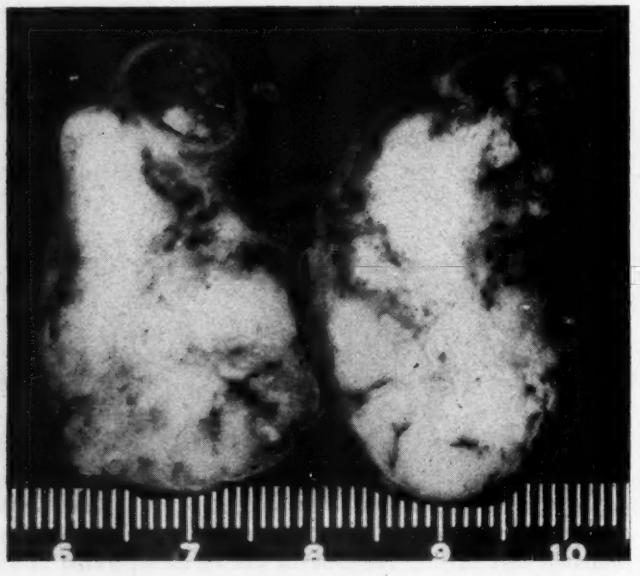

Fig. 1.—Gross section of the tube showing the outgrowth of the tumor from the tubal lumen, on the right.

In 1949 and 1950 the patient had further surgery to remove the pseudomucinous material. I first saw her in June, 1951. The chest and extremities were very thin from emaciation, but the abdomen was greatly distended by the same material to such degree that the patient was dyspneic. Under general anesthetic the abdomen was opened in the midline. About 8,000 to 10,000 c.c. of material resembling consommé were removed. Due to the many pockets caused by adhesions, complete evacuation was impossible. The abdomen was closed with wire.

Hospital convalescence of the patient was uneventful and she was discharged feeling much better and still with slight drainage. Fortunately for the patient, a fistula developed in the abdominal wall through which she was able to express with difficulty some of the gelatinous material. This kept her from filling as rapidly as in the past so that I was not called to see her again until January, 1952. It was at that time that I first learned of the draining fistula.

Fig. 2.

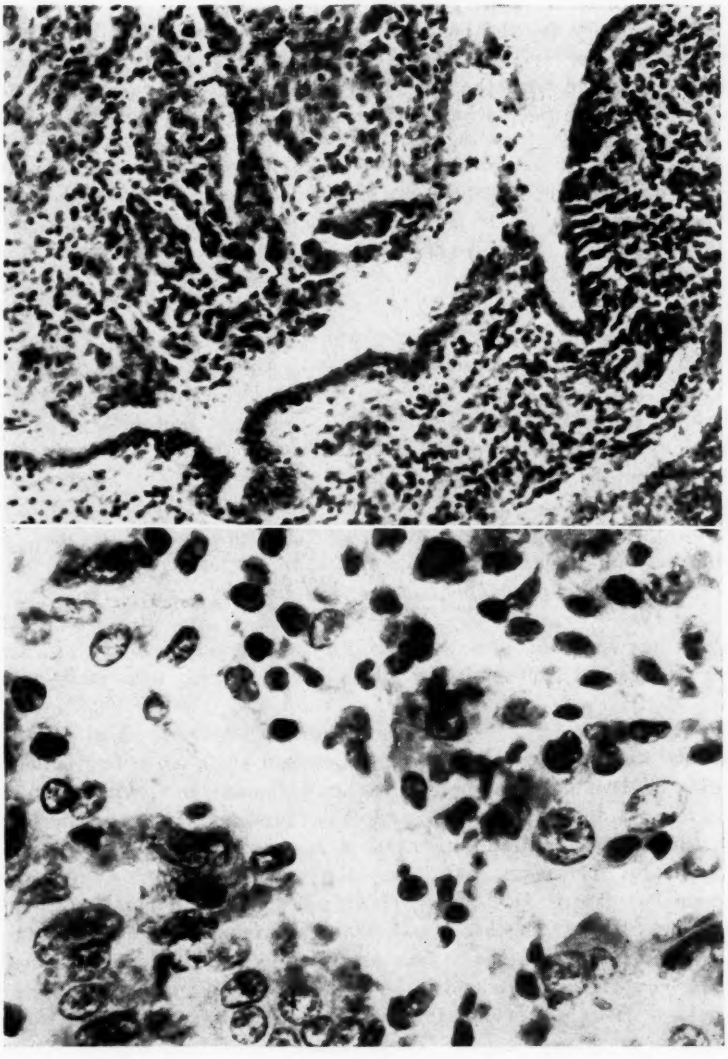

Fig. 3.

Fig. 2.—Anaplastic adenocarcinoma contiguous with the tubal epithelium. Chronic inflammation in the tubal wall. (×258.)
Fig. 3.—High power of the tumor. (×900.)

According to current literature the material of the cyst is said to contain large amounts of hyaluronic acid. With this in mind, 1,500 T R (turbidity reducing) units of Wydase (lyophilized hyaluronidase) dissolved in 10 c.c. of distilled water were placed in the abdominal cavity through a small midline incision above the umbilicus. A large, hard,

fixed tumor was palpated in the pelvis extending to the umbilicus. About forty-eight hours after the instillation of Wydase the patient was greatly excited by the flow of about 2 gallons of fluid through the opening of the fistula. This continued for several days. After the loss of so much fluid she was able to be ambulatory for the first time in several years. The effects of the Wydase lasted several weeks so that reinstillation has been necessary only once a month.

The primary tumor has not been affected by Wydase. However, there is no doubt by either the patient or her family that there is much more now to offer her for symtomatic relief from pressure of the pseudomucinous fluid. Whereas it had been necessary to undergo major surgery for the past four years, the current year is up with no thought of surgery for the future.

This case is reported with the hope that more experience can be gained in the treatment of these unfortunate people and less radical means can be offered to relieve them of their symptoms.

435 Waldron Building

ADENOCARCINOMA OF THE UTERUS WITH METASTASES TO THE UMBILICUS

E. A. Riemenschneider, M.D., and Richard L. Miller, M.D., Akron, Ohio

(From the Akron City Hospital)

CARCINOMA of the umbilicus, as either a primary or a secondary neoplasm, is of rather infrequent occurrence. Metastatic lesions to the umbilicus from adenocarcinoma of the uterus are even more rare. Cullen,[1] in his work on the umbilicus, reported that he had never seen this latter condition, although he quotes two such case reports from the French literature. Warner,[2] also mentions these two cases. A search of the records at Akron City Hospital has failed to reveal any such case.

This patient presented herself because of a growth in the umbilical region. She had noticed a 10 pound weight loss during the previous year and for three years there had been a scant periodic bloody vaginal discharge. She was admitted to Akron City Hospital, May 10, 1951, for diagnosis and treatment.

The umbilical ulcer first appeared in December, 1950. Whereas, at first appearance it was red, weeping, and flat, upon admission it appeared to be of granulomatous or neoplastic nature and was covered with a thick purulent crust. Secondary complaints included low back pain, ankle edema, and tenderness in the left calf.

Her past medical review was not remarkable. No digestive disturbances were noted and the stools were always normal in color, motion, and consistency. There was some history of exertional dyspnea, chronic cough, and pedal edema, but none of these conditions ever prompted her to seek medical treatment.

The laboratory findings on admission included the blood count and urine; the latter was entirely negative and the red blood count was 3,660,000, hemoglobin 10.5 Gm., with white blood count 8,900.

Physical examination revealed a well-developed, well-nourished, white woman, aged 65 years, well oriented and in no acute distress. Her general physical condition was fairly good and the only deviations from normal were a blood pressure of 180/110 associated with a soft mitral and aortic systolic murmur. The liver edge was palpable 4 cm. below the right subcostal margin. At the umbilicus was a fresh granulating lesion raised above the surface, approximately 3 cm. in diameter with secondary superficial infection. There were palpable subinguinal lymph nodes. The ankles were both grossly edematous and there were swelling, redness, and tenderness along the course of the left posterior tibial and greater saphenous veins with calf tenderness and a positive left Homans' sign. Pelvic examination was deferred until the following day when it was performed under anesthesia.

On May 11, 1951, the patient was taken to the operating room and, under Pentothal anesthesia, a pelvic examination revealed normal atrophic external genitals, the outlet, ducts, and glands were normal, the vagina clean and smooth and the cervix was mobile, in the midline, and clean. The corpus uteri was found to be approximately three times normal size with profuse bleeding issuing from the cervical os when dilated. A curettage was productive of nearly one ounce of friable neoplastic endometrium; therefore, a 50 mg. capsule of radium was inserted into the uterine cavity, vaginal packing applied, and a biopsy of the umbilical lesion taken before the patient was returned to her room.

These biopsy reports read as follows:

1. Umbilicus: Adenocarcinoma of histologic Grade II to III with focal metaplasia to squamous type. Chronic purulent inflammation with focal necrosis and fibrosis. This le-

sion appears to be neoplastic and infiltrates the subcutis and extends through the corium to the epidermis (Fig. 1).

2. Uterus: Adenocarcinoma of histologic Grade II to III with focal metaplasia to squamous type. The cell type is similar to that in the abdominal wall. There is focal necrosis, lipoidosis, and chronic purulent inflammation (Fig. 2).

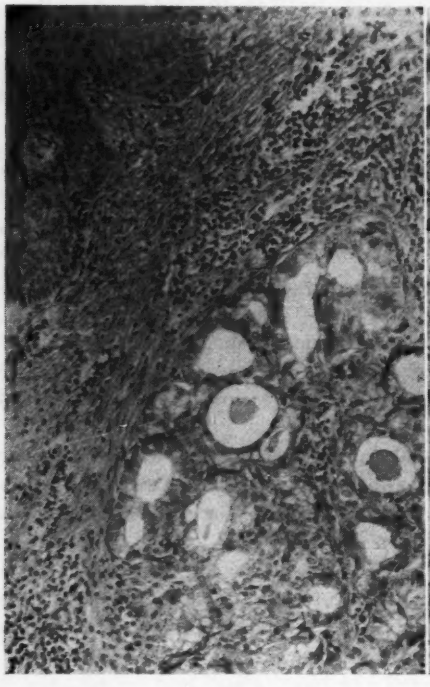

Fig. 1.

Fig. 2.

The patient withstood this minor procedure well and the radium was removed after she had received 5,000 mg. hr. The following day she was returned to her home. She was advised to have a hysterectomy within four to six weeks, but refused.

On Jan. 5, 1952, approximately seven and one-half months later, she was readmitted in a terminal stage with a diagnosis of generalized carcinomatosis. The umbilical lesion was not much enlarged grossly, but large tumor masses could be palpated throughout the entire abdominal cavity and open lesions were evident over the subinguinal lymph node metastases. The patient was stuporous and totally unresponsive. The red blood count was 1,910,000 hemoglobin 4 Gm., 26 per cent. She was given narcotics p.r.n. and approximately twenty-four hours later she died quietly.

The significant findings at autopsy were as follows:

Gross: The umbilicus was replaced by an ulcerated nodule 5 cm. in length, composed of soft reddish-gray tissue. The pelvic organs were rather markedly enlarged and bound down in firm adhesions, including the large bowel and small intestine. The uterus was asymmetrical and markedly enlarged and it measured 9 cm. above the level of the symphysis. The liver was 3 cm. below the xyphoid process. The gross cut sections revealed metastases throughout the liver, large intestine, mesentery and mesenteric lymph nodes, as well as the aortic and retroperitoneal lymph nodes. The inguinal nodes were replaced by metastases.

Microscopic: Adenocarcinoma histologic Grade II to III involving the uterus, with a primary site in the endometrium and the secondary metastases involving the umbilicus,

regional lymph nodes, large bowel, small intestine, liver, and lateral pelvic wall (Figs. 1 and 2).

Comment.—It is felt that the significant finding which makes this case of interest is that there was no demonstrable gross nor microscopic anatomical extension between the uterine and umbilical lesions and these two sites were separated by a space measuring about 8 cm. This represents a true metastasis either blood or lymphatic borne from an adenocarcinoma of the uterine endometrium to the umbilicus significant because only two previous recorded cases have appeared in the medical literature.

When a uterine growth extends to the umbilicus, it is presumed that it usually follows the lymphatics found in the course of the remnants of the obliterated hypogastric arteries and urachus upward to the umbilical depression.

Our sincere thanks to Robert L. Faulkner, M.D., for his helpful criticism.

The photomicrographs shown are the product of the Dr. Walter A. Hoyt, Photography Laboratory of Akron City Hospital.

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POSTPARTUM ECLAMPSIA OCCURRING ON THE FIFTEENTH POSTPARTUM DAY*

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(From the Department of Obstetrics and Gynecology of Louisiana State University School of Medicine and Charity Hospital of Louisiana, at New Orleans)

POSTPARTUM eclampsia occurring during the day of delivery or on the first day following delivery is a relatively common clinical entity. On the other hand, eclampsia developing later than the second postpartum day is quite rare and requires verification by every means including clinical and laboratory data and exclusion procedures before the diagnosis becomes tenable.

Stander[1] was obliged to revise his opinion that eclampsia never occurred more than seventy-two hours after delivery. He presented in detail three cases representing eclampsia occurring on the fourth, sixth, and eighth days, respectively, following delivery. The clinical and laboratory data from these three cases paralleled conclusively the accepted findings in eclampsia.

The case reported here has permitted us to conclude that eclampsia can occur as late as the fifteenth postpartum day.

The patient (L. M. L.), a 20-year-old Negro woman, was first seen in the prenatal clinic during her first pregnancy in 1949. She had a completely normal prenatal course without evidence of pre-eclampsia and had an uneventful labor with delivery of a normal female child on Jan. 8, 1950. The postpartum course following this pregnancy was complicated by the development of hypertension (blood pressure 150/100) first noted six weeks following delivery. Her blood pressure gradually decreased to 140/90 three months after delivery and was not recorded again until a normal pressure of 114/80 was obtained in the ninth month after delivery. Concomitant with this, the diagnosis of early pregnancy was made.

The prenatal course during this second pregnancy was uneventful, except for the presence of proteinuria during the last three weeks of pregnancy. The highest blood pressure recorded during the nine prenatal clinic visits was 130/80. There was a total weight gain of 24 pounds. The estimated date of confinement was June 22, 1951. She was admitted to the hospital in early labor on June 27, 1951. Physical examination at this time was entirely within normal limits. The blood pressure was 120/75. Laboratory findings were within normal limits, except for the presence of a "trace" of albumin in the initial voided urine sample. The patient was somewhat anemic as shown by a packed cell volume of 26 mm. A normal 8 pound, 10 ounce, female child was delivered spontaneously after an uncomplicated 20 hour labor. The blood pressure shortly following delivery was 130/75. A catheterized urine sample obtained several hours after delivery contained no albumin or reducing substances. The patient was discharged to her home on the second postpartum day.

The patient felt perfectly well at home until thirteen days after delivery when she began to experience "headaches and dizzy spells." These became progressively more severe and on the following day were associated with two violent attacks of vomiting. She then noted some swelling of the face. On the fifteenth postpartum day, July 13, 1951, the headaches and dizziness became more severe. According to her husband she was lying in bed when she suddenly "became stiff and began to twitch and shake violently." She was brought to the hospital by ambulance in a semicomatose state, 30 minutes after the convulsion.

*Aided in part by the Edward G. Schlieder Educational Foundation of New Orleans, La.

On admission the patient was stuporous and there was some edema about the face. The blood pressure was 180/120 and the pulse 78 per minute, temperature 99.2° F.

There was neither muscle rigidity nor spasm. All tendon reflexes were normal. Blood studies performed at this time revealed a packed cell volume of 35 mm.; blood urea nitrogen of 23.5 mg. per cent; uric acid of 4.3 mg. per cent; chlorides of 579 mg. per cent; serum protein of 6.2 Gm. per cent and carbon dioxide of 40 vol. per cent. The urine contained 2 plus albumin. Shortly after admission she was given morphine sulfate intramuscularly and Sodium Amytal intravenously.

Three hours after admission a lumbar puncture was performed. An initial cerebrospinal fluid pressure of 200 mm. of water and a closing pressure of 160 mm. of water were the only noteworthy findings.

Basal sedation with phenobarbital sodium was begun. The blood pressure remained in the 180/110-120 range. Twelve hours after admission the patient had a generalized convulsion. Sodium Amytal was immediately given intravenously. At this time the blood pressure was 180/104 and the pulse was 120 per minute. The packed cell volume had increased to 40 mm.; the uric acid to 5.0 mg. per cent; and the serum proteins to 6.85 Gm. per cent. The urine contained no albumin. During the following four hours, two episodes of minor muscular twitchings were observed and each time Sodium Amytal was given intravenously.

The urinary output for the first 24 hours after admission averaged 70 c.c. mm. per hour with a variation of 50 to 100 c.c. per hour.

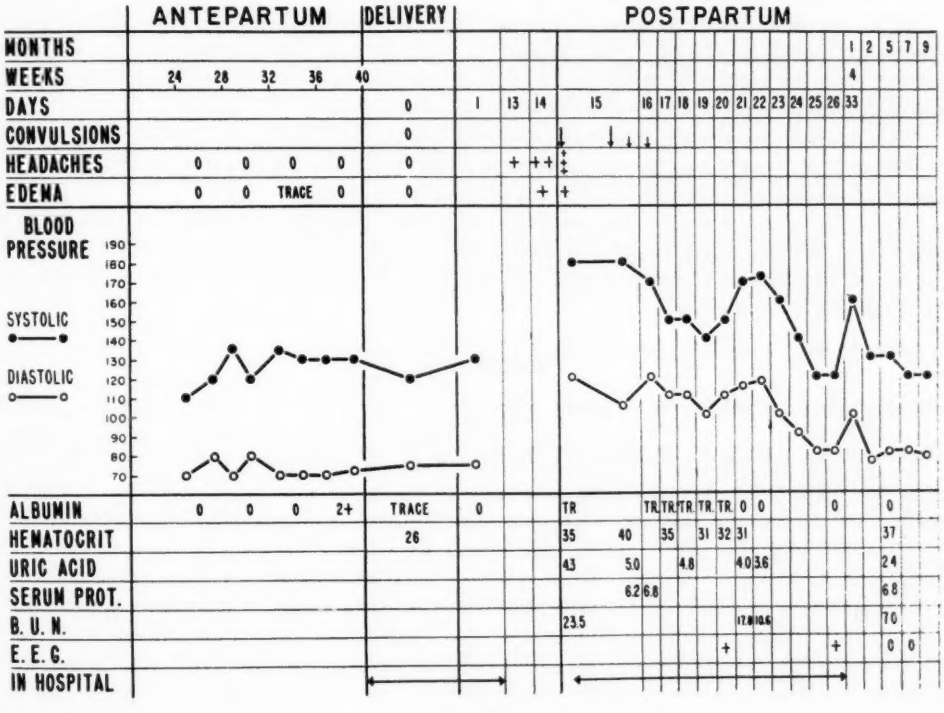

Fig. 1.

Electroencephalography performed on the fifth postconvulsion day indicated a convulsive disorder on the basis of diffuse brain damage. Thirteen days later, a second electroencephalogram indicated marked improvement, but still showed residual diffuse brain damage. By the time the second electroencephalogram was obtained, the blood pressure had returned to a normal level of 120/80.

Proteinuria disappeared on the sixth day after admission. On this day the laboratory findings were as follows: packed cell volume 31 mm.; uric acid 4.0; blood urea nitrogen 17.8. Blood pressure at this time was 170/114.

The effect of tetraethylammonium chloride was studied on two separate occasions while the patient was still manifesting hypertension during her hospitalization. The method of administration and dosage suggested by Garber and associates[2] was followed. There was no decrease in blood pressure during the study interval. On the contrary the blood pressure increased significantly and this elevation persisted for approximately one hour on both occasions before returning to the initial control level. Her blood pressure gradually returned to 120/80 and the patient was discharged from the hospital on the twenty-sixth postpartum day, July 28, 1951.

She has been followed in the outpatient clinic at stated intervals for nine months. For the first three months following her discharge there was an increase in blood pressure to 150/90. The pressure then gradually returned to the 120/70-80 range during the second three-month interval and has remained at this level up to the present time. Pertinent laboratory data were obtained during the fifth postpartum month. The packed cell volume was 37 mm.; uric acid was 2.4; blood urea nitrogen was 7.0, and the serum protein was 6.8. Electroencephalography was repeated in the fifth and again in the seventh month revealing complete recovery without evidence of residual damage.

The laboratory data obtained from this patient are represented graphically in Fig. 1.

The electroencephalographic data obtained are similar to those reported by Jost,[3] who concluded that the electroencephalographic pattern in the eclamptic patient returns to normal as clinical improvement is manifested by a drop in blood pressure. He found no specific pattern characteristic of eclampsia.

It is of considerable academic interest that tetraethylammonium chloride consistently produced an elevation of the blood pressure in this patient. No explanation is offered for this effect, but the failure of the drug to cause a decrease in pressure may lend substantiation to the diagnosis of true eclamptogenic toxemia of pregnancy.

This patient apparently does not represent the clinical entity designated by Kaltreider and Gilbert[4] as "early unexpected puerperal hypertension," since the hypertension of this patient was associated with proteinuria, edema, and convulsions.

It is felt that because this patient manifested rapidly developing hypertension associated with edema, convulsions, and coma, as well as proteinuria, hemoconcentration, elevated blood urea nitrogen and uric acid, the diagnosis of eclampsia occurring on the fifteenth postpartum day is confirmed.

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AN UNUSUAL MONSTROSITY

Parasiticus Tetrabrachius Rachipagus Tetrapus Diophthalmos Triotus

J. N. PANNULLO, M.D., NEWARK, N. J.

(From the Presbyterian Hospital)

MRS. N. J. was 31 years of age, para i, gravida ii. The previous family and personal history were irrelevant. The expected date of delivery was Oct. 3, 1948.

On July 28 a diagnosis of polyhydramnios with twin pregnancy was made as two fetal hearts were heard.

The patient went into labor September 16, and after a 3½ hour labor this freak in right sacroposterior position, weighing 5 pounds, 8 ounces, was delivered with very little difficulty. The second child was delivered by version and breech extraction and was perfectly normal.

The freak lived 3½ days.

Flat x-ray showed the same bony attachments as reported in the autopsy. Barium given by mouth entered a stomach and was passed by the parasite about twenty hours later. After six hours some barium appeared in the intestines of the host who passed a minute quantity of barium a few seconds before death. Genitourinary x-rays were inconclusive though both the host and parasite voided.

The necropsy findings by Dr. Samuel Goldberg, Pathologist of the Presbyterian Hospital, were as follows:

Attached to the parietal bone of the host and beneath the skin posterior to the right ear are several cervical vertebrae. The two small arms of the parasite are joined at the ear of the host, and this has only a rudimentary opening. There are two fingers on each hand, the fourth and the fifth.

On the anterior chest of the host there is attached a pelvis and 2 formed legs, attached to their respective thighs, and movable.

The external genitals and the ani of both the parasite and the host appear normal.

The sternum is absent but the manubrium is present.

Head: The brain of the host is quite large and congested—otherwise normal.

Chest: The left chest contains a normal-sized thymus. The right chest also contains a thymus though smaller in size. There is a single larnyx-pharynx and trachea. The epiglottis is split into two parts, one part normal, the other part jagged. In the right chest there is a normal lung with three lobes, while in the left side the lung is irregular in shape, containing 2 lobes much larger than normal and markedly congested. There is a normal bifurcation of the trachea.

Heart: The host has two hearts; the left heart is normal in size and contains two ventricles, a septum, and two auricles. The foramen ovalis is closed. There is a patent ductus arteriosus. The arch of the aorta is on the left side of the trachea. The right heart is much smaller and contains two chambers, a ventricle and an auricle. From the ventricle there is an artery forming an arch on the right side of the trachea to the aorta. The right and left pulmonary arteries emanate from the ductus arteriosus. There is a single normal thoracic and abdominal aorta.

There are one esophagus and one stomach. There is an accessory spleen 2 cm. in diameter in the omentum near the other spleen which is normal in size.

There are two livers fused together at the upper border. There are two normal gall bladders, one in each liver.

There are two pancreata, the left being larger.

There is one duodenum markedly enlarged at the point where the pancreatic and the bile ducts enter it.

There is one jejunum. At the beginning of the ileum there is an inverted Y-shaped anastomosis, one ileum going toward the parasite terminating in a short colon and rectum, while the other branch continues to the cecum-appendix-colon and rectum of the host. In the ileum of the parasite is a short Meckel's diverticulum.

Fig. 1.

The host has two kidneys and two adrenals, normal in size, shape, and location. The parasite has one kidney bulging out in the pelvis. There is a vestigial adrenal gland adjacent to it.

The urachus is closed in both the host and parasite.

The parasite has one urethra and a bladder.

In the pelvis of the parasite is a uterus but no tubes or ovaries. The vagina and urethra are normal.

All the pelvic organs of the host are normal.

365 Roseville Avenue

Department of Book Reviews

EDITED BY PHILIP F. WILLIAMS, M.D., PHILADELPHIA, PA.

Review of New Books

Obstetrics

This little compendium on the anatomy of the human pelvis[1] is the outgrowth of the author's experience in teaching applied anatomy to surgical residents and to others with similar needs. It is a practical book, not intended to replace the detailed descriptions of the standard textbooks. Neither is it a digest or condensation of the textbooks, since much of the text and the best of the illustrations are based on special dissections used for teaching purposes. Chapters are allocated to the organic systems, including both the male and female reproductive systems, with special emphasis on the surgical significance of each.

There is interesting material on the growth and sex differentiation of the bony pelvis and well-documented description of the various pelvic types in the female. Some sections in the book are much too brief. With the general interest in cancer of the cervix the reader is disappointed to find so small space allocated to the pelvic lymphatics in the female.

Many of the illustrations are copies or modifications of standard anatomical line drawings. The best of the illustrations are excellent original drawings based on regional dissections. These fine studies are somewhat marred because the names and guides are thinly printed and are not read with ease.

This book will have little value for the experienced surgeon, but well fulfills its purpose of providing informative detail for review or refresher courses.

EARL T. ENGLE

This concise monograph, **Diabetes and Pregnancy**,[2] should be most helpful to every physician practicing obstetrics. The authors have divided diabetes into the mild, moderately severe, and severe forms and have stressed that the long-standing or severe form presents the most difficult problem during pregnancy. It is this type that is most often associated with premature sclerosis, hypertension, and nephritis, that confuse the picture and may be mistaken for pre-eclampsia complicating the pregnancy. The authors feel that the incidence of toxemia of pregnancy is no more common in pregnancy with diabetes than in nondiabetic pregnant women.

The management of the diabetic pregnant patient consists of stabilization of carbohydrate metabolism at a level which will prevent symptoms, achieve and maintain normal body weight, develop a "sense of well-being," and avoid acidosis, coma, and hyperinsulinism.

Under Chapter XI, hormone therapy is discussed and series of cases studied by well-known authors throughout the country are cited, which were treated with and without hormone

[1]**The Human Pelvis.** By Carl C. Francis, M.D., Assistant Professor of Anatomy, Department of Anatomy, Western Reserve University, Cleveland, Ohio. 210 pages with 61 illustrations. St. Louis, 1952, The C. V. Mosby Company. Price $5.00.

[2]**Diabetes and Pregnancy.** By Ralph A. Reis, M.D., Professor, Obstetrics and Gynecology, Northwestern University Medical School; Edwin J. DeCosta, M.D., Assistant Professor, Obstetrics and Gynecology, Northwestern University Medical School; M. Davis Allweiss, M.D., Associate in Medicine, Northwestern Medical College. 78 pages. Springfield, Ill., 1952, Charles C Thomas. Price $2.50.

therapy with no appreciable difference in the end results. The conclusion is that extensive endocrine therapy seems unwarranted on both theoretical and practical grounds. Finally, the dangers to the baby born of a diabetic mother are hypoglycemia, anoxia, lethargy, and prematurity, and each one of these newborns, regardless of actual age, size, and weight, should be cared for as a premature.

This book is well written in simple descriptive language and should be particularly advantageous to the obstetrician and pediatrician.

R. E. NICODEMUS

Dr. Johnstone has written a timely and interesting account of William Smellie's[3] professional life and the part he played in the development of modern obstetrics. One regrets, with the author, that for a man whose attainments were so outstanding, so little is known of his early training and of his private life in the heyday of his maturity. Dr. Johnstone states that Smellie began to practice in his native Lanark without any evidence of degree or licensure, but believes some of his training was obtained at Glasgow. Apparently, a large part of his country practice was in obstetrics, since the carefully recorded notes of complicated cases of those years are constantly met in his Collection of Cases. Smellie's removal from Lanark to London was prompted, according to Dr. Johnstone, by a desire for further training, but a study of the London system of teaching seems to have filled him with the idea he could do a better job than the obstetric teachers he heard and watched in the metropolis.

The period of his life in London is very thoroughly presented. Dr. Johnstone has had access to the recently available *Journal of Dr. Peter Camper* of Leyden, who was a pupil of Smellie in 1748 and again in 1752, and who contributed several plates for the *Anatomical Tables.* Camper's notes on Smellie's system of clinical teaching on the free home delivery service and on his homemade manikins are fully utilized in this book. This Dutch student was enthusiastic over Smellie. Dr. Johnstone discusses Smellie's first boarder in London, Dr. William Hunter, and the relationship of these men over a long period of time, when both practiced in London. Smellie's methods and success led to certain professional jealousies which the author fully describes.

A discussion and analysis of Smellie's writing form the bulk of the text. The *Treatise,* which appeared in 1751, was, in the opinion of Dr. Johnstone, a new and positive contribution to midwifery. It contained Smellie's most famous writing, his description of the mechanism of normal labor. In this description, Smellie made a series of statements, wholly new and which controverted all previously expressed obstetrical opinions. Dr. Johnstone also points out that Smellie early adopted a conservative attitude in the management of the third stage. He describes Smellie's use of the forceps, his models, and does not feel Smellie was too quick in their application, an unjust criticism made by many later writers.

Selection of cases from the *Collection* for further elucidation of Smellie's theories and practice is admirable. The concise clinical histories and the sound common-sense deductions well illustrate Smellie's mastery of his subject. Dr. Johnstone gives a fascinating chapter on Dr. Burton's attack on Smellie. Dr. Burton gained immortality, writes the author, as "Dr. Slop" in Tristram Shandy; Dr. Smellie, as the Master of British Midwifery. The part Smellie played in developing the forceps, and its use in this period, is well told.

Dr. Johnstone closes his account of Smellie by reviewing the scant material regarding his last few years, a few autobiographical fragments mentioning Smollett and Hunter, and a splendid tribute to this Scot, who, self-made, became one of the greatest figures in obstetrics.

PHILIP F. WILLIAMS

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[3]**William Smellie. The Master of British Midwifery.** By R. W. Johnstone, M.D., Professor-Emeritus of Midwifery and the Diseases of Women, University of Edinburgh. 139 pages with 30 illustrations. Baltimore, 1952, The Williams & Wilkins Company. Price $4.00.

Culdoscopy—A New Technic in Gynecologic and Obstetric Diagnosis[4] is intended to prepare the gynecologist who wishes to include this technique in his diagnostic regime. The material includes, in addition to a complete discussion of culdoscopy, sections on colpocelio-centesis, pneumoperitoneum, and roentgenography. The clearly presented methods for examining the pelvis through the posterior cul-de-sac are amply illustrated by black and white drawings, photographs, and roentgenograms. Potential complications are discussed and methods indicated to avoid them.

The use of the culdoscope in evaluating specific lesions such as tubal pregnancy, endometriosis, and tubal patency, and in the management of closed tubes is discussed. It is doubtful that many gynecologists will share the author's enthusiasm for overdistending blocked tubes until they rupture or of puncturing weak areas in the distended tubal wall through the culdoscope.

In general, the monograph serves its avowed purpose adequately and should certainly be carefully studied by any gynecologist who considers the use of culdoscopic examination.

J. ROBERT WILLSON

In this handbook on gynecology,[5] the author has deviated considerably from the usual plan and has presented the material with a strong surgical viewpoint. One-fourth of the book is devoted to a thorough consideration of preoperative preparation and postoperative care and complications. The remainder is devoted to illustrations and drawings which show essential steps in operative technique. The operations are arranged in an orderly manner, first those on the vulva and perineum, next those on the vagina and cervix, and finally the abdominal operations on the uterus and adnexa.

The section on preoperative evaluation and care stresses the importance of a careful history and physical examination. Among others the more common diseases and conditions which present problems to the gynecologist are diabetes, heart disease, obesity, and the care of the aged patient.

The section on postoperative care and complications deals with water balance, nutrition, early ambulation, shock, hemorrhage, blood transfusion, transfusion reactions, antibiotic and chemotherapy, phlebothrombosis and thrombophlebitis, pulmonary complications, urinary retention and urinary tract infections, postoperative distention, intestinal obstruction, wound complications, and peritonitis. As the author states, parenteral fluid therapy resolves itself into three periods: preoperative, operative, and postoperative. The fluid and electrolyte needs for each patient should be individualized. There are three general types of parenteral fluids: (1) water and electrolyte, (2) nutritional fluids, and (3) fluids to combat or prevent development of shock, such as plasma and whole blood. Rule-of-thumb procedures are extremely undesirable in giving parenteral fluids because the surgeon should estimate the needs of each patient and in this way subsequent mortality and morbidity will be decreased. One should always keep in mind the importance of early oral feeding and return to partial or complete general diet as soon as possible postoperatively. The author warns about the harmful effect of too much fluid administration. It is well known that this tendency to continue parenteral feeding may prolong and make more difficult the maintenance of normal body water, electrolyte, caloric, and nitrogen balance when simply the shifting to oral feeding will return the patient to physiologic homeostasis.

In the preoperative preparation the use of the cardioscope should be mentioned as this is of great value when operating on a poor-risk patient.

The caliber of the drawings is an attractive feature and the lettering is clear. This makes it easy to follow the steps of a surgical procedure. The illustrations are black and

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[4]**Culdoscopy—A New Technic in Gynecologic and Obstetric Diagnosis.** By Albert Decker, M.D., D.O.G., F.A.C.S., Clinical Professor of Gynecology and Obstetrics, New York Polyclinic Medical School and Hospital; Associate Attending Physician in Gynecology and Obstetrics, New York Polyclinic Hospital; Attending Gynecologist, Knickerbocker Hospital. 148 pages with 50 illustrations. Philadelphia, 1952, W. B. Saunders Company.

[5]**Surgical Gynecology.** By J. P. Greenhill, M.D., Professor of Gynecology, Cook County Graduate School of Medicine; Attending Gynecologist, Cook County Hospital; Attending Obstetrician and Gynecologist, Michael Reese Hospital. 350 pages with 101 plates showing 495 illustrations. Chicago, 1952, The Year Book Publishers. Price $8.50.

white. The plates are excellent because of their clarity and accuracy. Certain minor omissions are noted, such as the Vernon David technique for closure of a small rectovaginal fistula.

In the experience of this reviewer, the combination of Watkins-Wertheim operation and Manchester operation has been of value in older patients having poor fascia in the anterior vaginal wall. Another minor omission is the dilatation of the cervical canal following cautery treatment of the cervix, conization of the cervix, or amputation of the cervix. A useful addition to the Gilliam technique for uterine suspension is the advancement of the vesicouterine flap as shown by Te Linde. This was not mentioned. The handbook is certainly up to date as it shows the various steps in radical panhysterectomy with bilateral lymphadenectomy. This is one of the more radical surgical procedures in vogue today.

This book obviously deals with one branch of gynecology—surgery. The experience and ability of the author as a worker and teacher in the field of surgical gynecology are evidenced throughout the drawings. The author is to be congratulated on having prepared a volume which is decidedly helpful to the young gynecologist and trainee.

JOSEPH A. HEPP

This monograph[6] concisely and clearly reviews the known facts concerning the seasonal and estrous reproductive cycles of vertebrates, and analyzes those factors which appear to determine, control, or affect them. The reproductive cycles of fishes, amphibians, birds, reptiles, fur-bearing and domestic animals, and primates are all discussed. The effects of such environmental factors as temperature and day length, and of food supply and domestication are examined.

The chapters dealing with the relationship of hormones to reproduction and sexual behavior provide a basic understanding of well-established facts.

The book is fairly well documented and should be on the required reading list for all students in the biological sciences.

R. A. KELSER

While this treatise is, from its title, ostensibly limited to **Functional Endocrinology,**[7] only from birth to adolescence, much of its content is applicable to the problems of endocrinology in general, regardless of the age of the patient.

To begin this review with a minor criticism, while hiding behind my back the bouquets which I shall later throw in the authors' direction, I question whether their concepts of the age periods which they include in their consideration would be generally accepted in their entirety. There will certainly be no argument about "birth," nor probably about their concept of the notoriously difficult-to-define adolescence, as indicating "the whole period of childhood during which sexual differentiation occurs," although just about this definition would, by most gynecologists at least, be given for "puberty." The latter, on the other hand, is stated by the authors (page 302) to refer "to the moment at which reproduction becomes possible, i.e., in the female, the first ovulation." If this be true, the not infrequent girls of 17 or 18, who after the age of 13 or 14, have had anovulatory but otherwise fairly normal menstrual cycles, and who have had for a number of years large and well-developed breasts, axillary and pubic hair, well-rounded feminine figures, well-developed external genitals, and a well-developed puberal uterus, would still be considered subpuberal. I believe that this is an incorrect definition, aside from the matter of its practical utilization, for we are certainly not going to submit girls to biopsies, basal temperature studies, or insemination to establish the ovulation which the authors consider the criterion of puberty.

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[6] **Vertebrate Sexual Cycles.** By W. S. Bullough, D.Sc., Sorby Research Fellow of the Royal Society of London. New York, 1951, John Wiley & Sons, Inc. Price $1.50.

[7] **Functional Endocrinology—From Birth Through Adolescence.** By Nathan B. Talbot, M.D., Associate Professor of Pediatrics, Harvard University; Physician, Children's Medical Service, Massachusetts General Hospital. Edna H. Sobel, M.D., formerly Research Fellow in Pediatrics, Harvard University; at present Instructor in Pediatrics, University of Cincinnati College of Medicine. Janet W. McArthur, M.D., Instructor in Gynecology, Harvard University. John D. Crawford, M.D., Instructor in Pediatrics, Harvard University. 638 pages with 253 illustrations. Cambridge, 1952, Harvard University Press. Price $10.00.

This criticism is of small moment in comparison with the many virtues of the book. It is divided into 11 chapters, although who wrote which is not stated. The authors, however, make a harmonious team, as is indicated by the fact that essentially the same plan of presentation is followed in all the chapters. The chief subdivision in each is into Basic Considerations and Clinical Considerations. The endocrine glands considered are in order: the thyroid, the parathyroids, the adrenal cortices, the adrenal medullae, the ovaries, the testes, the anterior pituitary, the posterior pituitary, and the pancreatic islets. A short but worth-while Appendix is devoted to blood, p'asma, or serum values, urine values, miscellaneous tests, and units of measurement. Very wisely the authors have not included any discussion of the pineal body and thymus, formerly included, always nebulously and probably unjustifiably, among the endocrine glands.

The chapter on the thyroid includes a good summary of the physiology of that gland and of the present status of the medical and surgical treatments of hyperthyroidism. Incidentally, it includes also a good discussion of the far less generally recognized hyperthyroidism due to primary pituitary dysfunction, as well as a note of caution concerning the fallibility of basal metabolic tests in children.

The two chapters devoted to the adrenals embrace 160 pages, which is not surprising in view of the wealth of material made available by the recent intensive interest in this formerly neglected treasure-trove of the endocrinologists. Much of this discussion involves complex problems of organic chemistry. As an example of the completeness of the authors' review, no less than 13 tests are given for the respective rates of production of the various types of adrenocortical hormones.

The chapter on the ovaries is probably the one in which gynecologists and obstetricians would be most directly interested. It is a good one, although, in truth, it does not contain a great deal more information than can be found in a good modern textbook of gynecology. The authors put far more stress on vaginal smear studies and hormone determinations in the study of functional disorders than would be considered practicable or even necessary by most gynecologists.

In the two excellent chapters devoted to the pituitary it seems curious not to find at least some mention of Sheehan's work on the various types of hypopituitarism which have excited interest among obstetricians especially. Whatever the authors might think on this subject, at least some discussion of the "Sheehan syndrome," as it is now being called, would have been welcome.

This book is beautifully made, with a clear and easily readable type, and it has obviously been well edited. Only two mistakes of spelling were noted by the reviewer. Hydrometrocolpos is misspelled hydrometrocalpas on page 346, and the anatomist Gartner's name is misspelled Gärtner on page 365, a very common error. The illustrations are adequate but not numerous, and quite a number have been borrowed from other publications.

All in all, the authors have done an outstanding job with this book, and its appeal should be, and probably will be, much wider than the chronologic limitations implied in its title might lead one to believe.

EMIL NOVAK

Dr. Emil Novak's **Textbook of Gynecology,**[8] which for several years has been a standard text of wide usefulness, now makes its first appearance in Spanish translation. As is well known, the book makes no attempt to provide details of operative technique; it is, rather, a systematic compendium of the pathology, diagnosis, and nonsurgical treatment of gynecologic disorders, discussed with the author's well-known thoroughness and sound conservatism. Dr. Longoria's translation is a very close approximation of the factual content of the original text, and conveys the subject matter clearly and usably; only occasionally

[8]**Texto de Ginecologia.** By Emil Novak, M.D., F.A.C.S., Assistant Professor Emeritus of Gynecology, Johns Hopkins Medical School. Edited by Dr. Gustavo Cuervo Rubio, Professor of Gynecology, University of Havana. Translated into Spanish by Dr. Gerardo Amargos Longeria. First Edition in Spanish. 876 pages with 484 illustrations. Havana, Cuba, 1952, M. V. Fresneda.

does the meticulously literal rendering result in stylistic infelicity. The format of the volume, although above average for South American publications of this type, falls far short of customary standards of publication prevalent in the United States. The numerous and pertinent illustrations lose much of their potential usefulness as a result of poor reproduction; the colored illustrations are particularly unsatisfactory. The binding is sturdy but somewhat unsightly. Nevertheless, the mere availability to Spanish-speaking students and practitioners of the textual material is timely and desirable, and this standard work will unquestionably constitute a most useful addition to their libraries.

DOUGLAS M. HAYNES

This small volume[9] is a compendium of the authors' technique in vaginal surgery. They prefer the vaginal approach whenever feasible, emphasizing the importance of proper instruments and of a well-trained assistant.

The body of the work is a compact and thorough description of surgical technique, with many illustrations. Every step of every procedure is illustrated in great detail. The text is brief and easily readable.

Vaginal plastic procedures, per se, are not described. The repair of rectocele is omitted. Uterine interposition is described, but with the notation that it is not an operation for prolapse.

The authors attack ovarian cysts, large myomas, and ectopic pregnancy from below. If there are extensive pelvic adhesions, the uterus is bisected longitudinally and each half removed with its adnexa.

Opinions differ as to the indications for the vaginal approach. The latter is used much more extensively by the authors than is common in this country. Nevertheless, this excellent book may be read with interest and pleasure by every gynecologist.

BRUCE A. HARRIS, JR.

"For some time Gynecology has gone beyond the narrow frame of the genital sphere and surgical therapy. It has become a vast and precise specialty with its indispensable disciplines: biology, medicine, surgery, physiology, endocrinology, radiology, to which we must add obstetrics with its strict rules and exigencies, as well as the mammary physiopathology, another aspect of the genital life of woman.

"The tremendous strides of biology in recent years have brought about a sort of revolution in gynecology. The practitioner who gives a good part of his daily duties to female pathology must be au fait of the actual trend in this field."

In such terms, Laffont expresses himself and presents his **Manuel de Gynécologie**[10] to his readers in his Foreword. It is written in comprehensible language for the student. It covers the subject in its entirety, yet it stresses very little of the surgical possibilities. In fact, where surgery is indicated it does not always state the ideal type of operation to be performed in each particular case. On the other hand, medical therapy, hormone therapy, and physiotherapy are discussed considerably, too much sometimes in the opinion of the reviewer. Illustrative descriptions of applications of radium for the treatment of carcinoma of the cervix, or elaborate paragraphs on electrotherapy seem to us an incentive and an encouragement for the practitioner to undertake such methods of treatment for office use, when we believe it should be left to the specialist in therapeutic radiology. The social aspect of diseases is discussed under the headings of such diseases, becoming an integral part of each chapter. Touching mostly on the French viewpoint it does, nevertheless, cover, by comparison, what exists in other countries.

The illustrations are schematic for the greater part; they complete admirably the text and render the more difficult descriptions easily understandable.

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[9]**Die vaginalen Bauchhöhlen-Operationen.** By Prof. Dr. P. Werner and Dr. J. Sederl, Vienna. 52 pages with 120 illustrations. Vienna-Innsbruck, 1952, Urban und Schwarzenberg. Price DM 46 ($11.00).

[10]**Textbook of Gynecology (Manuel de Gynécologie).** By A. Laffont, Professor of Obstetrical and Gynecological Clinic at the Faculty of Medicine of Algiers. 606 pages with 203 illustrations. Paris, 1952, Masson & Cie. Price 2650 francs.

An elaborate index and a detailed table of contents make references readily traceable.

Notwithstanding the above remarks, we consider this book the best of its kind published in French on gynecology for the practitioner and the student since the war.

LÉON GÉRIN-LAJOIE

This is not a textbook, as such, but a concise didactic exposé[11] in thirteen theoretical lessons specially compiled for the author by some of his students. The general practitioner may find in it a refresher reference on some particular subject but the student will peruse it with advantage in preparation for his examinations in Gynecology.

Following a Foreword and an Introduction, the chapters are suggestive of what may be found in this brief book: how to make a diagnosis; hemorrhages in gynecology; leukorrheas; pain; metritis and cervicitis; anomalies of position of uterus; prolapse; cysts of the ovary; fibromyomas; adnexitis; most frequent genital carcinomas; solid tumors of the ovary; hormonal treatments.

No photographs or sketches or tables illustrate the text. It is a weakness and we deplore the brevity of some paragraphs, particularly on the question of therapy. But the author does not claim to have touched all of the problems that can be encountered by the practitioner but only the most frequent gynecological disorders that are met in everyday practice.

LÉON GÉRIN-LAJOIE

[11] **Some Aspects of Present-Day Gynecology (Quelques aspects de la Gynécologie Actuelle).** By R. Bourg, Professor at the Free University of Brussels, Chief of the Brugmann University, Department of Gynecology and Obstetrics. 188 pages. Paris, 1951, Masson & Cie. Price 900 francs.

Correspondence

The Variability of the Vascular Supply to the Ureter

To the Editor:

Since we have conducted an investigation similar to that reported in the April number of your JOURNAL (Vol. 63, No. 4, p. 774) we should like to have the opportunity of commenting on this contribution. Our article, "The Blood Supply to the Lower End of the Ureter and Its Relation to Wertheim's Hysterectomy," appeared in the *Journal of Obstetrics and Gynaecology of the British Empire,* Vol. 58, No. 4, August, 1951, p. 609.

Dr. Varverikos credits Sampson with the earliest complete study of ureteral blood supply, although this is not the case, since Haller (1749) in his *Iconum Anatomicarum,* Fascic. IV, gave an excellent account, whilst Feitel (1901), an associate of Wertheim, carried out an extensive study on the blood supply of the pelvic ureter some 150 years later.

The use of latex preparations is considered by Dr. Varverikos to be without the disadvantage of causing venous filling. Using a similar technique of injection into the thoracic aorta for the study of the arterial supply of the pelvic ureter, we found that the most satisfactory media were "Chlorbismol" (May & Baker) for displaying the larger vessels, and Indian ink for demonstrating the finer vessels and the marked anastomoses that occur between them on the ureteric wall. Although we tried latex preparations initially, we discarded these on the grounds that the degree of filling was inadequate as compared with that of the other two media. We also observed that all three injection masses frequently passed into the pelvic veins and often the finest venous radicles were partially injected. This venous overspill could be diminished but not eliminated by ligation of the renal vessels and presumably was due mainly to the juxtamedullary shunt in the kidney and not to the passage of the injection mass through the capillary bed ("Chlorbismol," for instance, has a particle size of about 12μ which is larger than the diameter of a capillary). The inefficacy of the latex injection mass is well demonstrated in the figures shown in this article, particularly Figs. 1 and 4, in which the ureters appear comparatively avascular, a deficiency which is not encountered with Indian ink.

It would be interesting to know how many foetal and infant specimens of each sex were examined; no comment is made on this. The findings, however, bear a resemblance to those described by us, first, as regards the constancy of the terminal ureteric supply from the uterine artery—in our series it was absent in only 4 out of 42 ureters examined—and, second, as regards the suggestions made by one of us (Racker) of ligating the uterine artery medial to the ureter in Wertheim's hysterectomy to preserve the terminal ureteric supply from this source. Dr. Varverikos' statement that in a third of his specimens the uterine artery affords the only source of supply to the terminal ureter is difficult to reconcile with our findings. We constantly found at least one additional vessel, the source of this being from the vaginal artery, the superior vesical artery, or the caudal branch of the internal iliac artery, and often a combination of these. The internal iliac supply was found frequently in our series, and we are in accordance with the opinion expressed previously by Meigs that it is important to preserve this vessel also, in the course of a Wertheim's hysterectomy. The fact that we used different injection media and controlled pressures of around 150 mm. Hg may account for these discrepancies.

Dr. Varverikos comments on the fact that the most constant vessels to the ureter are at its two extremities, yet no reference is given to any vessels supplying the upper end of the ureter either in the text or the figures of his paper. The intermediate supply is said

to be inconstant, but this seems to be at variance with his findings that a branch from the common or internal iliac artery is present in 60 to 65 per cent; this vessel, of course, is "the middle ureteric artery" first described by Haller (1749). The points raised concerning the magnitude and distribution of these intermediate vessels would depend on the degree of filling, itself dependent on the patency of the vessel, the pressure of injection, and the type of injection mass used. In our series the ureteric anastomoses were so well marked that it was felt that no reliable comment could be made on this point. The only observation in this respect that might have been made concerns the comparative calibres of the parent ureteric arteries, but as these vessels also afford a supply to the surrounding connective tissues and related peritoneum, as Dr. Varverikos points out in his article, only a rough assessment can be made on the ratio of territory of ureteric supply to the diameter of the vessel.

We are in agreement with Dr. Varverikos that an intermediate vessel may be sacrificed without impairing the blood supply to the ureter but not for the reasons he gives. The most important factor enabling division of intermediate vessels is the rich supply to the intermediate part of the ureter from the ascending branches of the terminal ureteric vessels.

Finally, the suggestions put forward in reference to incisions of the peritoneum are similar to those made by Feitel (1901) some fifty years ago.

J. L. Braithwaite, M.D.
D. C. Racker, F.R.C.S.E., F.R.C.O.G.

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Department of Anatomy
University of Liverpool
August, 1952

Reply by Dr. Varverikos

To the Editor:

In reply to the letter containing the critical essay of Dr. Braithwaite of the University of Liverpool, I hasten to make one point clear and that is: the *complete* essay which I submitted for my M.Sc. at McGill University is at the said University Library in Montreal.

This work was begun in the fall of 1949 and progressed under the direction of Professor C. P. Martin of the Department of Anatomy. The material—of which the paper under discussion is only a *part*—is still in the McGill Department of Anatomy and Museum. The finished essay was presented to and marked by Professor Martin, Dr. A. E. Campbell, and Professor N. W. Philpott of the Department of Obstetrics and Gynaecology of McGill University.

In the original work I believe Dr. Braithwaite will find a great number of points which he brings out, or which he finds lacking in my paper. We regret that in the publication of our work we had not come across his material in the *Journal of Obstetrics and Gynaecology of the British Empire.*

E. D. Varverikos, M.D.

Vancouver General Hospital
October 15, 1952

Item

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology will hold the next scheduled examinations (Part II), oral and pathological, for all candidates at the Edgewater Beach Hotel, Chicago, Ill., May 17 through May 24, 1953. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Requests for re-examination in Part II must be made prior to Feb. 1, 1953, submitting data regarding additional training or experience and medical school or hospital staff appointments acquired in the interim.

Inquiries relative to residency training should hereafter be directed to Lawrence M. Randall, M.D., Assistant Secretary, American Board of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minn., who is in charge of residency training for the Board.

Application forms for Appraisal of Incomplete Training, for Certification, and requests for current Bulletins should be made to:

ROBERT L. FAULKNER, M.D., SECRETARY
AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY,
2105 ADELBERT ROAD, CLEVELAND 6, OHIO

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